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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service • National Institutes of Health • National Cancer Institute

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EPIDEMIOLOGY AND ETIOLOGY OF HUMAN LYMPHORETICULAR MALIGNANCIES: VIRAL STUDIES

1. NATURAL ANTIBODIES TO THE HUMAN T CELL LYMPHOMA VIRUS IN PATIENTS WITH CUTANEOUS T CELL LYMPHOMA.

Posner LE, Robert-Guroff M, Kalyanaraman VS, Poiesz BJ, Ruscetti FW, Fossieck B, Bunn PA, Minna JD, Gallo RC
Lab. Tumor Cell Biology, NIH, Bethesda, MD, 20205
J Exp Med; 154(2):333-346 1981

Serum samples were obtained from patients with cutaneous T cell lymphoma (CTCL) and leukemia, and from 55 normal random donors. Retroviruses HTLV-CR (grown in HUT 102 cells) and HTLV-MB, isolated from patients CR and MB, respectively, were used, along with several other retroviruses. The sera were screened for the presence of natural antibody to HTLV-CR, using a solid-phase radioimmunoassay. Sera from patient CR and one other patient reacted specifically with proteins of HTLV-CR. CR serum also reacted with HTLV-MB proteins. Solid-phase immunocompetition and competition radioimmunoprecipitation assays demonstrated the specificity for HTLV-CR proteins. Patient CR antibodies were directed against viral core proteins with mol wt of 24,000 and 19,000, as shown by radioimmunoprecipitation analysis. Some reactivities to other animal retroviruses, including the baboon endogenous virus, simian sarcoma virus, feline leukemia virus, and gibbon ape leukemia virus, were demonstrated. These reactivities apparently were not virus-specific, but related to cellular antigen contamination of viral preparations or to antigens in fetal calf serum. The results indicate for the first time a specific antibody reaction to a retrovirus in humans. (38 Refs)

2. FAMILIAL ACUTE MYELOGENOUS LEUKEMIA ASSOCIATED WITH RNA VIRUS AND POLYMORPHISM OF 1QH+.

Sadamori N, Nonaka H, Ichimaru M, Igarashi H, Hirota M, Sawada H
Dept. Genetics and Endocrinology, Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
Cancer Genet Cytogenet; 4(1):23-30 1981

In order to investigate the genetic background of leukemogenesis of two brothers with acute myelogenous leukemia (AML), they and their family members were studied genetically, immunologically, virologically, and cytogenetically. Their parents were first cousins once removed and had the same or a very close type of human WBC antigen (HLA) and blood groups. In all five non-leukemic family members the IgG level was elevated, and in two healthy siblings the IgM level was beyond the normal range. The RNA reverse transcriptase activity in serum of the younger brother (Case 2) with AML was elevated. A cytogenetic study of the family revealed polymorphism of 1qh+. Based on these findings, we discuss the genetic and environmental factors of familial leukemia. (Author abstract) (24 Refs)

3. REACTIVITY OF ANTISERA TO ANTIGENS OF C-TYPE VIRUSES WITH LEUCOCYTES FROM PATIENTS WITH ACUTE LEUKAEMIA.

Pullen S, Hersey P
(c/o Hersey) Kanematsu Memorial Inst., Sydney Hosp., Macquarie St., Sydney, Australia 2000
Pathology; 13(2):289-298 1981

A number of previous studies have suggested that certain C-type viruses from non-human primates are associated with acute leukemia in humans. The present study sought to examine this association further by detection of antigens related to these viruses on the surface of acute leukemia cells. Antisera against the whole viruses or the major internal protein of simian sarcoma, endogenous baboon and Rauscher viruses were tested against mononuclear cells from patients with acute leukemia at various stages of their disease in 51Cr release WBC dependent cytotoxic assays. A high proportion of the patients had antigens related to these viruses detectable on their blood WBC at some stage in their disease whereas with one exception blood WBC from non-leukemic subjects did not. The expression of these antigens did not show a close relation to the number of blast cells in blood detected on morphological grounds. Antigens related to the non-human primate viruses were detected on mononuclear cells from bone marrow samples of several non-leukemic patients which indicated they were not specifically associated with leukemia. Antigens related to the Rauscher virus were detected on cells of practically all bone marrow samples tested. These results suggest that assays to detect these antigens would be of limited usefulness to monitor disease activity in patients with acute leukemia. Their expression on blood WBC however appeared strongly associated with acute leukemia and further studies to assess the prognostic and epidemiological significance of detection of these antigens appears warranted. (Author abstract) (16 Refs)

4. NEW CONCEPTS IN NUTRITION AND CANCER: IMPLICATIONS FOR FOLIC ACID.

Butterworth CE
Dept. Nutrition Sciences, Univ. Alabama, Birmingham, AL, 35294
J Dent Child; 48(4):300-303 1981

Many of the proposed mechanisms by which diet and nutrition may be related to cancer seem to involve a genetic or chromosomal injury that may be conditioned by nutritional factors such as folic acid (FA). Hormone-induced localized nutrient deficiency has been postulated as a mechanism involved in the development of cervical dysplasia in women taking oral contraceptives (OCs). In a clinical trial, FA supplementation led to the regression of OC-induced cervical dysplasias in women who continued to take OCs. No such regression occurred in placebo-treated women, some of whom developed carcinoma in situ. The concept of nutritionally dependent fragile sites and somatic mutations on human chromosomes is not supported by clear evidence that chromosomal fragility is involved in carcinogenesis. However, a combination of chromosomal fragility and deficiencies of FA or another essential nutrient may account for specific mutations in target tissues. One published report describes 34 cases of serious hematologic disease (including 5 acute leukemias) in a family with an inherited defect of cellular FA uptake. Cervical cancer is circumstantially linked to a DNA virus (herpesvirus), and several RNA viruses are known to be oncogenic in animals. The retroviruses induce RNA-directed DNA synthesis via reverse transcriptase. There is good reason to su spect that FA-containing coenzymes play an important role in this DNA synthesis, as they do elsewhere. Folacin plays an important role in the infection

of Escherichia coli by T-even bacteriophages. FA and its analogs may play a similar role in viral oncogenesis. (17 Refs)

EPIDEMIOLOGY AND ETIOLOGY OF HUMAN LYMPHORETICULAR MALIGNANCIES: OTHER STUDIES

5. INCREASED LEUKEMIA, LYMPHOMA, AND SPONTANEOUS ABORTION IN WESTERN NEW YORK FOLLOWING A FLOOD DISASTER.

Janerich DT, Stark, Green, Burne, Jacob, McCus
Bureau Cancer Control, New York State Dept. Health, Albany, NY, 12237
Public Health Rep; 96(4):350-356 1981

The incidences of leukemia and lymphoma in river valleys and non-river valleys of western New York and in the rest of New York were studied for the yr 1966 to 1977. The incidence of spontaneous abortions in the same areas was studied for the yr 1970 to 1977. Background radiation levels from several areas of concern, including water sources, were measured during 1978-9. No unsafe levels were found. In June 1972 the river valleys surveyed were severely affected by flooding from a tropical storm. Until 1974 the incidence of leukemia and lymphoma was the same throughout the area studied. In 1974-77 there was a slight increase throughout upstate New York, but a much larger increase in the river valleys. The z test showed the difference to be significant (P less than 0.05). Distribution of cases by sex, age, or tumor type was unchanged. In the last quarter of 1972 and into 1973, a significant (P less than 0.01) excess of spontaneous abortions occurred. The increases in the rates of the diseases studied could not be linked to radiation. Suggested causes include acquaintance networks, exposure to sylvatic or wildlife virus, and substantial psychological or physical stress. (16 Refs)

6. GASTRO INTESTINAL LYMPHOMAS: A RETROSPECTIVE ANALYSIS.

Saksena A, Shankur R, Rajvanshi VS
Dept. Pathology, G. S. V. M. Medical Coll., Kanpur, India
Indian J Cancer; 18(2):123-127 1981

Between 1969 and 1979, 48 lymphomas of the gastrointestinal (GI) tract were identified out of 426 cases of lymphomas. Most of the 48 GI lymphomas were of the non-Hodgkin's group (79.17%) with 20.83% in the Hodgkin's disease group. Approx half of the cases were restricted to the second and third decades; only 12.5% presented after 50 yr. All age groups showed a male preponderance. Most patients presented with signs of intestinal obstruction, progressively increasing abdominal lump, and loose motions. Wt loss and anorexia were common. The primary sites were the ileum (35.4%), colon (20.8%) and only one case (2.08%) occurred in the duodenum. Grossly, approx 60% showed a diffuse infiltration of the intestinal wall with flat, greyish-white, plaque-like lesions and concomitant loss of mucosal pattern. The draining mesent eric lymph nodes were enlarged in 75%. Follicular hyperplasia with a sinus reaction of lymph nodes was found in half of the cases, and the specific lesion in the other half. Hodgkin's disease was the mixed cellularity type, while the non-Hodgkin's lymphomas were lymphocytic lymphoma, poorly differentiated type (33.3%) and lymphocytic lymphoma, intermediate differentiation (22.9%). The clinicopathologic findings and their relation to possible etiological factors were discussed. (17 Refs)

7. PEDIGREE ANALYSIS OF HODGKIN'S DISEASE IN A NEWFOUNDLAND GENEALOGY.

Thompson EA
The Statistical Lab., 16 Mill Lane, Cambridge CB2 1SB, England
Ann Hum Genet; 45(3):279-292 1981

To test the pattern of inheritance for Hodgkin's disease (HD), a pedigree analysis of three close communities of Newfoundland was carried out. Of 1,743 individuals, a total of 1,521 individuals were found to be descended from a single couple. Of 21 cases of lymphoreticular diseases recorded, 10 had HD or generalized immunodeficiency (ID). Detailed analysis of the ancestry of HD/ID cases and computations of such cases indicated a simple recessive susceptibility. Malignancies other than HD or ID were not associated with this susceptibility. (12 Refs)

8. AN ITALIAN SURVEY OF CANCER IN SIBLINGS.

Carli M, Cordero di Montezemolo L, De Rossi G, Fiandino G, Fossati-Bellani F, Fugardi MG, Guazzelli C, Haupi R, La Dogana R, Lovati C, Madon E, Mancini A, Mandelli F, Massimo L, Milici G, Rebuffi L, Robino G, Rosi A, Rossi MR, Rubbi P, Russo A, Severico R, Schiliro G, Tamaro P, Zanazzo G, Zurlo MG

(c/o Patore, G.) Catedra di Epidemiologia dei Tumori Umani, Istituto di Anatomia e Istologia Patologica, via Santena 7, 10126 Torino, Italy

Minerva Pediatr; 33(10):449-451 1981

Up to now 29 families were identified with two or more children who developed cancer before they were 14 yr old (27 families with 2 cases, one each with 3 and 4). In 14 families both children developed the same type of cancer. The family with three cases all had leukemia and the family with four cases two had Hodgkin's lymphoma, non-Hodgkin's lymphoma was found in one and one had leukemia. (8 Refs) (In ITA)

9. IS THERE A GENETIC BASIS FOR THE DIFFERENCES IN CANCER INCIDENCE BETWEEN AFRO-AMERICANS AND EURO-AMERICANS?

Goldson A, Henschke U, Leffall LD, Schneider RL

Dept. Radiotherapy, Howard Univ. Hosp., 2041 Georgia Ave. NW, Washington, DC, 20060

J Natl Med Assoc; 73(8):701-706 1981

The data of the Third National Cancer Survey show for many cancer types, large differences in cancer incidence between Euro-Americans and Afro-Americans. As in other racial studies, it is difficult to separate environmental and genetic factors. For the cancers which are more frequent among Afro-Americans, environmental factors seem to be primarily responsible. However, among the cancers less frequent in Afro-Americans, there are some for which the racial differences have a genetic basis. This is clearly the cause for skin and lip cancers caused by UVB of the sun. Genetic factors are probably also responsible for the racial differences in the incidence of malignant melanomas, testis cancers, astrocytomas, and Ewing's sarcomas. Perhaps there is also a genetic basis for some of the racial differences in the incidence of malignant lymphomas and leukemias. For all these cancers, Afro-Americans are less susceptible. The only cancer to which Afro-Americans appear more susceptible on the basis of genetic makeup is fibrosarcoma. This is in accord with the high frequency of keloids, a benign counterpart of fibrosarcoma in Afro-Americans. (Author abstract) (9 Refs)

EPIDEMIOLOGY AND ETIOLOGY OF NON-HUMAN LEUKEMIA AND LYMPHOMA

10. NATURAL KILLER CELL ACTIVITY IN A POPULATION OF LEUKEMIA-PRONE WILD MICE (MUS MUSCULUS).

Scott JL, Pal BK, Rasheed S, Gardner MB
(c/o Gardner) Dept. Pathology, Univ. California Sch. Medicine, Davis, CA, 95616
Int J Cancer; 28(2):241-247 1981

Natural cell-mediated cytotoxicity against YAC-1 targets was measured in splenocytes from leukemia-prone wild mice trapped near Lake Casitas (LC) in southern California. Cytotoxicity was mediated by cells that were non-adherent to nylon wool, non-phagocytic and resistant to thy-1.2 antiserum plus complement. Natural MuLV viremia in LC mice did not impair splenic cytotoxicity against YAC-1 target cells. Cells infected with amphotropic and ecotropic MuLV of wild mouse origin were not appreciably lysed by LC splenic effectors. Although variable levels of cytotoxicity were detected against YAC-1 by normal LC spleen cells, consistently low levels of cytotoxicity against allogenic LC lymphoma, sarcoma and carcinoma targets were found using the same splenocytes. These results indicate that LC mice possess splenocytes with the characteristics of natural killer (NK) cells as defined in inbred mice. The resistance of LC-derived targets to lysis by LC NK cells suggests that NK cells may not be involved in natural tumor immunosurveillance or that the development of spontaneous tumors may involve escape from NK-mediated effector mechanisms. (Author abstract) (46 Refs)

11. MILK OF DAIRY COWS FREQUENTLY CONTAINS A LEUKEMOGENIC VIRUS.

Ferrer JF, Kenyon SJ, Gupta P
Univ. Pennsylvania Sch. Veterinary Medicine, New Bolton Center, Kennett Square, PA, 19348
Science; 213(4511):1014-1016 1981

Milk or viable milk cells collected from 24 dairy cattle naturally infected with bovine leukemia virus were inoculated into lambs, which were subsequently examined for the development of infection. With this bioassay, infectious virus was demonstrated in the milk of 17 of the cows. Bovine leukemia virus is leukemogenic in at least two mammalian species, is widespread in commercial dairy herds, and can infect a wide range of hosts in vivo and cells, including human cells, in vitro. (Author abstract) (25 Refs)

12. CORRELATION OF BLOOD LYMPHOCYTE NUCLEAR POCKET PREVALENCE WITH ENZOOTIC BOVINE LEUKEMIA P24 VIRAL ANTIBODY TITERS.

Weber A, Bingham C, Pomeroy K
Dept. Veterinary Biology, Univ. Minnesota, St. Paul, MN, 55108
Am J Vet Res; 42(8):1395-1399 1981

The quantitative relationship between radioimmunoassay serotiters to p24 enzootic bovine leukemia viral antigen and the prevalence of lymphocytic nuclear pockets (LNP) was studied in 554 clinically normal dairy cows and bulls. Of the animals, 69% were seronegative. Of the seronegative animals, 44% had no observed LNP, whereas 93% of the seronegative animals had less than 1% LNP. However, 2.3% of the seronegative animals had substantially increased (greater than 2%) numbers of LNP, and conversely, 24% of the seropositive animals had no observed LNP. Statistical evaluation of the data, using contingency table and regression methods, provide significant (p less than 0.0001) evidence for a positive association between LNP prevalence and p24 bovine leukemia viral serotiters. Although significant, the association was weak, and hence LNP number had little value for predicting serotiter. (Author abstract) (23 Refs)

13. ESTABLISHMENT AND PROPAGATION OF A BOVINE LEUKAEMIA VIRUS-PRODUCING CELL LINE DERIVED FROM THE LEUKOCYTES OF A LEUKEMIC COW.

Mamoun RZ, Astier T, Guillemain B
Unite 117, Institut National de la Sante et de la Recherche Medicale, Unite 117, 229, cours de l'Argonne, 33076 Bordeaux, France
J Gen Virol; 54(part2):357-365 1981

A cell line (LB59Ly) derived from the WBC of a leukemic cow was established as a monolayer, which spontaneously released large amounts of a retrovirus. This virus was found to be indistinguishable from the bovine leukemia virus (BLV) produced by the commonly used high-producing heterologous cell line (FLK-BLV). Like the latter, its reverse transcriptase activity was greater in the presence of Mg++ cations than in the presence of Mn++ cations; its polyacrylamide gel electrophoresis pattern showed the presence of gp51, p24, p15, p12 and p10, and the antigenicity of the two major proteins completely cross-reacted with those of BLV from FLK-BLV cells. the virus was infectious and induced early and late polykaryocytosis, the specificity of which was demonstrated by use of specific anti-BLV sera. (Author abstract) (26 Refs)

14. COMPARISON OF VARIOUS SEROLOGICAL AND DIRECT METHODS FOR THE DIAGNOSIS OF BLV INFECTION IN CATTLE.

Gupta P, Ferrer JF
Section Viral Oncology, Comparative Leukemia Studies Unit, Sch. Veterinary Medicine, Univ. Pennsylvania, New Bolton Center, Kennett Square, PA, 19348
Int J Cancer; 28(2):179-184 1981

The sensitivities of several serological and direct methods for the detection of bovine leukemia virus (BLV) infection in cattle have been critically compared. Among the serological methods, the radioimmunoassay (RIA) using the BLV glycoprotein (gp) was found to be more sensitive than the RIA using the internal virion antigen (p25) and the immunodiffusion test using the virion gp antigen. The differences in sensitivity between these tests were particularly evident with sera of cattle in early stages of infection. The sensitivities of the syncytia induction assay and the competitive RIA for the direct demonstration of BLV infection in cattle are comparable. Following natural infection, antibodies to the gp antigen in most cattle were detected by the RIA several mo before infectious BLV became detectable by the SIA in the blood lymphocytes. It is concluded that the most accurate, sensitive, and rapid method for the detection of BLV infection in cattle is the RIA using the virion gp antigen. The data presented confirm that BLV infection as well as the antibody responses of naturally infected cattle to the BLV p25 and gp antigens are persistent. (Author abstract) (37 Refs)

CYTOGENETIC AND MORPHOLOGIC STUDIES

15. ABNORMALITIES OF CHROMOSOME NO. 1 RELATED TO BLOOD DYSCRASIAS: STUDY OF 10 CASES.

Miyamoto K, Hamasaki K, Kitajima K, Adachi T, Tanaka T, Sato J
Dept. Pathology, Cancer Inst., Okayama Univ. Medical Sch., Okayama 700, Japan
Acta Med Okayama; 35(2):137-141 1981

Cell lines and primary cells derived from patients with hematologic disorders were studied by chromosome banding techniques. Ten cases with nonrandom chromosomal abnormalities affecting chromosome 1q were found in 25 cases examined. The lymphoproliferative disorders included two cases of non-African Burkitt's lymphoma, two adult T-cell leukemias, one myelofibrosis, one chronic lymphocytic leukemia, one malignant lymphoma primarily in the brain, and three chronic myelocytic leukemias in blastic crisis. The partial karyotype of the 10 cases showed an excess of the long arm of chromosome 1: 2 had reduplication of partial regions of the long arm, 2 had an additional chromosome 1q, and the remaining 6 had translocation affecting the chromosome. The bands 1q25-q32 were found to be common excess regions in all the cases. Two cases showed partial tetrasomy of the specific region (q25-q32), seven showed partial trisomy, and one showed a mosaic of partial trisomy and tetrasomy. The break points on chromosome 1 were at centromere, q12, q21, q23, q25, and q32. The study indicated that involvement of the region (q25-q32) of chromosome 1 in translocation or duplication occurs not only in myeloid cells but also in lymphoid cells. (15 Refs)

16. PRESENCE OF THE PHILADELPHIA CHROMOSOME (PH(1)) IN POKEWEED MITOGEN STIMULATED L YMPHOCYTES DURING CHRONIC PHASE OF CHRONIC MYELOCYTIC LEUKEMIA (CML).

Juneja HS, Weiner R
Hematology-Oncology Div., Dept. Internal Medicine, Univ. Texas Medical Branch, Room MW 404, Galveston, TX, 77550
Cancer Genet Cytogenet; 4(1):39-44 1981

There has been a lack of direct cytogenetic studies on lymphocytes in the chronic phase of chronic myelocytic leukemia (CML). Peripheral blood mononuclear cells from seven patients in the chronic phase and one in the blastic phase of Ph1-positive CML were cultured in the presence of phytohemagglutinin (PHA) and pokeweed mitogen (PWM). Preparations adequate for analysis were obtained from eight PHA and five PWM stimulated cultures. Cytogenetic studies on the PWM stimulated cultured cells revealed, in one patient, the presence of the Philadelphia chromosome (Ph1) in 23/25 metaphases. The PHA stimulated lymphocytes from the same patient were all Ph1 negative. Lymphocytes from PHA and PWM stimulated cultures from the other six patients in the chronic phase and the one patient in blastic crisis were all Ph1 negative. The one positive result suggests that some B lymphocytes contain the Ph1 and that there is a common hematopoietic stem cell for B lymphocytes as well as the myeloid, erythroid, and megakaryocytic series. (Author abstract) (14 Refs)

17. CYTOGENETIC STUDILS IN CHRONIC MYELOGENOUS LEUKEMIA.

Carbonell F
Abteilung fur Klinische und Arbeitsmedizin, Universitat Ulm, Postfach 4066, 7900 Ulm, W. Germany
Sangre (Barc); 26(3):291-299 1981

Cytogenetic studies were performed on 45 cases of chronic myelogenous leukemia, 32 in the chronic phase, 8 in the acute phase, and 5 in both phases. Twenty-five patients were studied by the trypsin-Giemsa band technique and 20 with the Giemsa technique. The standard translocation, t(9;22) was identified in 24 of the cases studied by the band method. One case showed a complex translocation involving chromosomes 6, 9, 11 and 22. Alterations added to the Ph1 chromosome during the chronic phase were found in 19% of the cases. In the acute phase the karyotype alterations evolved in 87% of the patients, including, besides the Ph1 chromosome, a second Ph1, 17q isochromosome, and/or trisomy for chromosome 8. (Author abstract) (28 Refs) (In SPA)

18. CHROMOSOME CHANGES IN HUMAN CHRONIC LYMPHOCYTIC LEUKEMIA.

Schroder J, Vuopio P, Autio K
Folkhalsan Inst. Genetics, P.B. 819, SF-00101 Helsinki 10, Finland
Cancer Genet Cytogenet; 4(1):11-21 1981

Karyotypes were studied in B- and T-lymphocyte cultures from 66 patients with B-cell CLL and 2 patients with T-cell CLL. Thirty-one of the B-cell cases had not been treated for their disease; 35 had received radiotherapy, corticosteroids, or cytostatic drugs. Only one of the untreated patients had a clone with an abnormal karyotype. This was present in all her mitotic cells found in cultures containing lipopolysaccharide B (LPS, a B-cell mitogen) and 10% of those in cultures with pokeweed mitogen (PWM, a T- and B-cell mitogen). The karyotype of this clone was 46,XX,t(6;7),t(7;13),t(11;14). Four of the treated patients had clones with specific chromosome changes. These were 47,XY,+12 in 10% of leukoagglutinin (LA, T-cell mitogen) and protein A (PA, T- and B-cell mitogen) cultures in one case, 47,XX,+12.del(14) in 80% of LPS cultures and in all spontaneously dividing cells in another case, 46,XY,t(6;20) in all LPS cultures in another, and 46,XX,t(1;8) in all PA cultures in another. Both structural and numerical nonclonal chromosome aberrations (9%) were found in 24% of the different cultures of cells from untreated patients, and in 15% of the cells in 20% of the different cultures in the patient who had received treatment. Both patients with T-cell CLL had received treatment for their disease, and had a normal karyotype in all cultures. (Author abstract) (25 Refs)

19. ANALYSIS OF C BANDS IN HAEMATOLOGICAL DISORDERS.

Labal de Vinuesa M, Slavutsky I, Larripa I, De Salum SB
Instituto de Investigaciones Hematologicas 'Mariano R. Castex', Academia Nacional de Medicina, Pacheco de Melo, 3081, Capital Federal (1425), Argentina
Sangre (Barc); 26(3):319-323 1981

The variations in size and form of heterochromatin observed in normal populations are called polymorphisms. In patients with malignancies the number of such variations is increased. A study of the heteromorphism of chromosomes 1, 9, and 16 was performed in 20 normal subjects, in 32 patients with hematological malignancies and in 10 patients with preleukemia. Significant differences were found with respect to the control group in leukemia (p less than 0.001) and lymphoma (p less

than 0.05) but not in preleukemia. Chromosome 1 was characteristically involved, this being the only pair with differences with regard to the control group in leukemia and lymphoma; the pericentric inversion of the chromosome was the most remarkable finding. (Author abstract) (14 Refs) (In SPA)

BIOCHEMICAL, IMMUNOLOGICAL AND OTHER CELL BIOLOGY STUDIES

20. PRESENCE OF STRUCTURALLY ABNORMAL MOLECULES IN MONOCLONAL G IMMUNOGLOBULINS IN HUMAN MYELOMAS.

Malati T, Gupta RM, Chakravorty M
(c/o Gupta) Dept. Pathology, Inst. Medical Sciences, Banaras Hindu Univ., Varanasi 221005, India
Indian J Med Res; 73:930-937 1981

Monoclonal IgGs were isolated from the sera of seven patients with multiple myeloma by ammonium sulfate precipitation and DEAE cellulose column chromatography. Analysis of incidence of class and light chain type showed that three monoclonal proteins were IgG1 type K, three IgG1 type L and one IgG2 type L. Biochemical and biophysical studies revealed the presence of subnormal molecules in three out of seven cases. In one case, a rarely reported aggregated molecule of IgG having 10.32 S value was observed, while in another, a minor peak of a low mol wt IgG of 4.83 S was observed and in the third case, the entire myeloma protein was of low S value 3.94. No antibody activity could be detected against a variety of antigens tested for, including common human commensal and pathogenic flora. Further, there was a preponderance of lambda light chain monoclonal immunoglobulins. These observations lend support to the belief that the plasma cell malignancy in humans may result from genetic predilection rather than from chronic bacterial stimulation. (Author abstract) (23 Refs)

EXPERIMENTAL STUDIES INVOLVING CHEMICAL AGENTS AND IRRADIATION

21. DIFFERENCES IN SUSCEPTIBILITY TO THE CARCINOGENIC ACTION OF URETHANE IN HYBRID MICE (C57BL/6J X C3HF) F1 (B6C3) AND (C57BL/6J X BALB/C) F1 (B6C) (MEETING ABSTRACT).

Dragani TA, Sozzi G, Della Porta G
Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan, Italy
Tumori; 67(2,SupplA):59 1981

Beginning of the 10th day of life hybrid B6C3 and B6C mice were treated qod x 5 with ip urethane in dose of 1 mg/kg. The animals were kept under observation until they reached 8 wk of age. On macroscopic examination tumors were observed in more than 90 per cent of the animals treated. Thymic lymphomas appeared with greater frequency in the B6C3 hybrid with no difference between the sexes (54 per cent in the males, 62 per cent in the females). In the B6C hybrid this type of tumor developed more often in the females (17 per cent in the males, 28 per cent among females). Liver tumors were observed in both hybrids. They appeared sooner in the B6C3 than the B6C hybrid and no noteworthy differences between the sexes were observed whereas in the B6C hybrid females proved less susceptible. Macroscopic examination revealed lung tumors in just the B6C hybrid mice which were not especially susceptible to induction of this type of tumor (78 per cent in males, 68 per cent in females). Lung tumors were seen after the first yr of age when a considerable proportion of the B6C3 animals had already died as a result of thymic lymphomas or liver tumors. The preliminary data collected support the conclusion that both hybrids are especially suited to chemical carcinogeneis studies since they are susceptible to the induction of different types of tumors. The B6C3 hybrid inherits high susceptibility to liver carcinogenesis from its C3Hf father, while the B6C hybrid inherits its high susceptibility to pulmonary carcinogenesis from its BALB/c father. (no Refs) (In ITA)

22. RNA ONCOVIRUS EXPRESSION IN N-METHYL-N-NITROSOUREA-INDUCED LYMPHOMAS IN MICE.

Pinter A, Borzsonyi M
Natl. Inst. Hygiene, Budapest, Hungary
Int J Cancer; 28(2):219-223 1981

RNA oncovirus expression was investigated in thymic lymphomas induced by N-methy l-N-nitrosourea (MNU) in (C57BL/6 x DBA/2)F1(BDF1) mice. Out of 15 newborn mice injected with 20 mg/kg MNU, five developed thymic tumors of T-cell origin. Virus production of thymic cells from tumorous and normal animals was studied by an infectious center assay. All five tumors released ecotropic (mouse tropic) virus. No xenotropic or dual-tropic mink cell focus-inducing virus was found. No virus was obtained from thymus cells taken from six normal mice killed between 83 and 124 days; however, an ecotropic virus was cultured from the thymus of a 134-day-old normal mouse. According to these results, the MNU-induced thymic lymphoma development in BDF1 mice is accompanied by activation of endogenous ecotropic virus, whereas spontaneous activation also occurs in older mice. (Author abstract) (23 Refs)

EXPERIMENTAL STUDIES: DNA TUMOR VIRUSES

23. INITIATION POINTS FOR CELLULAR DEOXYRIBONUCLEIC ACID REPLICATION IN HUMAN LYMPHOID CELLS CONVERTED BY EPSTEIN-BARR VIRUS.

Oppenheim A, Shlomai Z, Ben-Bassat H
NCI, Bethesda, MD, 20205
Mol Cell Biol; 1(8):753-762 1981

Replicon size of two Epstein-Barr virus (EBV)-negative lymphoma cell lines, BJAB and Ramos, was measured, as in each of these lines converted by two strains of EBV, derived from the producer cell lines B95-8 and P3HR-1. Logarithmic cultures of randomly growing cells were labeled for 8 min with high-specific activity [3H]thymidine, the cells were gently lysed, and the DNA was spread on microscope slides and examined by autoradiography. In this manner, replication forks can be observed along the DNA fiber that became labeled during the radioactive pulse. Av replicon length was measured. Significantly shorter replicons (41, 21, and 54% shorter, respectively) were found in three of the four EBV-converted cell lines, BJAB/B95-8, Ra/B95-8, and Ra/HRIK, indicating that these cells had more initiation points than their EBV-negative parents. Replicons that were only slightly shorter than those of

the parents were found in BJAB/HRIK cells, although extensive track fusion occurred during the labeling of BJAB/HRIK. This implies that the true av replicon size of these cells was shorter than the observed value. It is suggested that EBV activates new initiation points for cellular DNA replication in EBV-transformed cells. (27 Refs)

24. PHYSIOLOGIC CONCENTRATIONS OF NORMAL HUMAN PLASMA LIPOPROTEINS INHIBIT THE IMMORTALIZATION OF PERIPHERAL B LYMPHOCYTES BY THE EPSTEIN-BARR VIRUS.

Chisari FV, Curtiss LK, Jensen FC
Dept. Clinical Res., Res. Inst. Scripps Clinic, La Jolla, CA, 92037
J Clin Invest; 68(2):329-336 1981

Epstein-Barr virus (EBV)-induced immortalization of adult human B lymphocytes is suppressed by physiologic concentrations of human plasma lipoproteins. Several inhibitory mechanisms appear to be operative. First, low density lipoproteins (LDL) directly reduce the ability of EBV to transform human B cells. Second, LDL as well as intermediate and very low density lipoproteins modulate early inductive events rendering the B cell refractory to transforming signals from EBV. Third, LDL also selectively inhibit an EBV-inducible step that occurs within 24 hr after transformation. Finally, very low density lipoproteins can abrogate the ongoing, cellular proliferation of EBV-transformed, established B cell lines. The plasma lipoproteins may therefore prevent the emergence of EBV-transformed malignant B cell clones in vivo. Conceivably, on this basis, environmental and genetic influences on plasma lipoprotein concentrations may affect the global distribution of Burkitt's lymphoma, a lymphoid malignancy putatively caused by EBV. (Author abstract) (28 Refs)

EXPERIMENTAL STUDIES: RNA TUMOR VIRUSES

25. ISOLATION OF TRANSPLANTABLE ERYTHROLEUKEMIA CELLS FROM MICE INFECTED WITH HELPER-INDEPENDENT FRIEND MURINE LEUKEMIA VIRUS.

Oliff A, Ruscetti S, Douglass EC, Scolnick E
LTVG, NCI, NIH, Building 41, Room D-240, Bethesda, MD, 20205
Blood; 58(2):244-254 1981

The Friend virus complex contains a helper-independent retrovirus, F-MuLV, and a replication-defective retrovirus, SFFV. Murine erythroleukemia cell lines (MEL) have been isolated previously from the leukemic tissues of mice infected with such stocks of Friend virus complex. Since our laboratory has shown that either F-MuLV or SFFV can induce a lethal erythroproliferative disease, it has been unclear which of the properties of conventional MEL cells were causally related to the infection of these cells by F-MuLV and which properties were related to the infection of these cells by SFFV. In this article, we have focused on the helper-independent component of the Friend virus complex, F-MuLV clone 57, which has recently been purified by molecular cloning. We report a method for the reproducible isolation of a new type of murine erythroleukemia cell that can be isolated from mice infected with F-MuLV clone 57. We have designated these cells as 57 TP-1, indicating their origin from mice infected with F-MuLV clone 57 and their characteristics as transplantable erythroleukemia cells. Upon sc, ip, or iv inoculation of these cells, 57 TP-1 cells grow in the hematopoietic organs of the recipient mice. No sc or ip nodules occur. Both F-MuLV and a Friend MCF virus can be detected in these cells, but no evidence of SFFV can be found. (Author abstract) (26 Refs)

26. CLONAL ANALYSIS OF THE LATE STAGES OF ERYTHROLEUKEMIA INDUCED BY TWO DISTINCT STRAINS OF FRIEND LEUKEMIA VIRUS.

Mager D, MacDonald ME, Robson IB, Mak TW, Bernstein A
Lab. Genetics, Univ. Wisconsin, Madison, WI, 53706
Mol Cell Biol; 1(8):721-730 1981

Differences between the tumorigenic colony-forming cells in the spleen of DBA/2J mice late after infection with the anemia-inducing strain of Friend leukemia virus (strain FV-A) and those present after infection with the polycythemia-inducing strain (FV-P) were explored. Hb and spectrin was found in cells within primary colonies derived from FV-A- and FV-P-transformed cells (CFU-FV-A and CFU-FV-P), suggesting that the CFU-FV-A and CFU-FV-P were transformed erythroid progenitor cells. In newly isolated cell lines from colonies of CFU-FV-P colonies, more than 25% of the cells contained Hb, while only 0-2% of cells from CFU-FV-A colonies contained Hb. In response to pure erythropoietin, many cells derived from CFU-FV-A colonies accumulated spectrin and Hb, while cell lines derived from CFU-FV-P did not. Primary CFU-FV-P colonies were diploid, while chromosomal aberrations were observed in the immediate progeny of CFU-FV-A. It is suggested that individual colonies from CFU-FV-A originated from single cells. Leukemic progenitor cells transformed by strain FV-A had the capacity to self-renew, while many of the corresponding cells transformed by FV-P did not, and as the disease progressed, the capacity of both strains to self-renew increased. A model for the multistage nature of Friend disease is proposed. (51 Refs)

27. ERYTHROLEUKEMIA INDUCING ISOLATES OF FRIEND LEUKEMIA VIRUS.

MacDonald ME
University of Toronto, Toronto, Ontario, Canada
Diss Abstr Int (B); 42(1):62-B 1981

Different isolates of replication-defective spleen focus-forming virus (SFFVA and SFFVP) and replication-competent murine leukemia virus (F-MuLVA and F-MuLVP) have been cloned from the anemia-(FV-A) and polycythemia-(FV-P) inducing isolates of Friend leukemia virus. Analysis of the biological properties of these viral isolates demonstrates that each of these genomes can induce erythroleukemia in susceptible mice. Both SFFVA and SFFVP have been rescued from rat fibroblast nonproducer cell clones by superinfection with F-MuLVA or F-MuLVP. These rescued viruses induce a rapid proliferative disease which is associated with the appearance of macroscopic spleen foci and splenic enlargement in genetically susceptible mice. The effects of SFFVA and SFFVP on host erythropoiesis, are distinct. SFFVP induces polycythemia and the appearance in the bone marrow and spleen of erythroid progenitor cells which can form colonies in serum-free culture medium in the absence of erythropoietin (EPO). In contrast, SFFVA induces anemia and a decrease in the number of EPO-dependent erythroid colony forming cells in the marrow and an increase in the number of EPO-dependent erythroid progenitor cells in the spleens of infected mice. The nature of the leukemia induced by clonal isolates of replication-competent Friend leukemia virus has also been investigated. F-MuLVA

and F-MuLVP both induce anemia and spleen enlargement when administered to newborn BALB/c mice. T he enlarged spleens of these mice contain an increased proportion of EPO-dependent erythroid progenitor cells and cells which contain the erythroid-specific membrane protein, spectrin. Taken together, these findings suggest that F-MuLVA and F-MuLVP induce erythroleukemia in newborn BALB/c mice which is similar to that induced in susceptible mice by FV-A. (no Refs)

28. TUMORIGENICITY, ANTIGENICITY AND IMMUNOGENICITY OF THREE MOLONEY LEUKEMIA VIRUS-INDUCED MURINE T CELL LYMPHOMAS.

Simon LL
Department of Health Sciences, Case Western Reserve University, Cleveland, OH
Diss Abstr Int (B); 41(11):4062-B 1981

C3HMT1820, C3HMT1892 and C3HMT1893, three in vitro adapted T cell lymphomas that arose in C3H/He mice infected with the Moloney strain of murine leukemia virus, differed in their ability to grow as tumors when injected into adult syngeneic mice. The cells of each of the lymphomas differed not only in their tumorigenic properties but also in their ability to stimulate the in vitro generation of allogeneic cytolytic cells. Likewise, they differed in their expression of H-2 encoded alloantigens and in their ability to suppress the generation of alloreactive cytolytic cells when present as third parties in allogeneic mixed lymphocyte cultures. Unless chemically modified with added haptenic determinants, none of the lymphomas was able to stimulate the generation of syngeneic cytolytic cells in vitro. C3HMT1820 cells, which readily produced tumors when injected into normal syngeneic immunocompetent mice, were both immunosuppressive and poorly immunogenic. C3HMT1892 cells were similar, but probably less immunosuppressive. In contrast, C3HMT1893 cells were neither immunosuppressive nor were they able to stimulate the generation of syngeneic or allogeneic cytolytic cells. This could be attributed to their lack of significant expression of H-2k encoded alloantigen. Nevertheless, C3HMT1893 cells were not tumorigenic in adult mice, suggesting that components of the immune system other than cytolytic T cells may be involved in their failure to produce tumors in adult syngeneic mice. In fact, C3HMT1893 cells were found to be susceptible to lysis by natural killer cells. (no Refs)

29. LEUKEMOGENIC PROPERTIES OF AKR DUALTROPIC (MCF) VIRUSES: AMPLIFICATION OF MURINE LEUKEMIA VIRUS-RELATED ANTIGENS ON THYMOCYTES AND ACCELERATION OF LEUKEMIA DEVELOPMENT IN AKR MICE.

O'Donnell PV, Stockert E, Obata Y, Old LJ
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Virology; 112(2):548-563 1981

The late preleukemic period in AKR mice (6-8 mo of age) is characterized by amplified expression of murine leukemia virus (MuLV)-related cell surface antigens on thymocytes. Analysis of thymic biopsies of preleukemic AKR mice at 180 days of age showed that antigen amplification was prognostic of spontaneous leukemia development within approx 100 days. In the present study we have investigated the viral basis of this preleukemic change in AKR thymus. Cloned isolates of ecotropic, xenotropic, and dualtropic MuLV that were derived from preleukemic or leukemic AKR thymus were tested by intrathymic injection of young AKR mice to determine which of the three classes of MuLV could induce antigen amplification, and, subsequently, accelerate leukemia development in the same animal. Only dualtropic MuLV exhibited these two activities in vivo. Considerable heterogeneity was observed among the 13 dualtropic MuLV isolates examined. In vitro three distinct serological phenotypes could be recognized on the basis of expression of MuLV gag gene-coded antigens GCSA and MuLV env gene-coded antigens GIX, G(RADA1), G(ERLD), and G(AKSL2) on the surface of infected cells. Virus isolates also differed in (i) relative ecotropic-xenotropic host range (dualtropism) as assayed by ratios of infectious titers on mouse and mink cells, (ii) induction of mink cell foci (MCF), and (iii) infectivity for NIH/3T3 cells.In vivo the two activities of antigen amplification and leukemia acceleration could be dissociated and thus represent distinct virus phenotypes. Seven isolates of dualtropic MuLV induced antigen amplification; these viruses encoded GIX, G(ERLD), and G(AKSL2) antigens, were MCF inducing, had SC-1/mink titer ratios of 0.4 or greater, and were infectious for NIH/3T3 cells. Only three of these virus isolates (MCF 247, MCF 69L1, and MCF 13) accelerated leukemia development. Analysis of dose-response relationships and kinetics of virus-induced antigen amplification by MCF 69L1 virus implicated virus infection of thymocytes in the preleukemic change. Moreover, the level of MuLV antigen expression on thymocytes at approx 1 mo postinjection of MCF 69L1 virus correlated directly with development of early leukemia. It is apparent that leukemia development in young AKR mice which can be induced experimentally by intrathymic injection of cloned isolates of dualtropic MuLV exhibits the hallmarks of spontaneous disease in this strain and thus can serve as a useful model for study of thymic leukemogenesis in mice. (Author abstract) (55 Refs)

30. WILD MOUSE ECOTROPIC MURINE LEUKEMIA VIRUS INFECTION OF INBRED MICE: DUAL-TROPIC VIRUS EXPRESSION PRECEDES THE ONSET OF PARALYSIS AND LYMPHOMA.

Hoffman PM, Davidson WF, Ruscetti SK, Chused TM, Morse HC
Veterans Admin. Medical Center, Dept. Neurology, Basic and Clinical Immunology and Microbiology, Medical Univ. South Carolina, Charleston, SC, 29545
J Virol; 39(2):597-602 1981

NFS/N mice inoculated at birth with an ecotropic murine leukemia virus (Cas-Br-M MuLV) obtained from wild mice developed hind limb paralysis beginning at 7 wk of age and nonthymic lymphomas beginning at more than 20 wk of age. Studies of 1-to 7-wk-old Cas-Br-M MuLV-infected mice showed the following: (i) a marked increase in nonecotropic MuLV-related antigens on spleen cells but not thymocytes beginning at 2 wk; (ii) the appearance of dual-tropic mink cell focus-forming (MCF) MuLV-related gp70 in spleen but not thymus or brain cells at 4 wk; and (iii) the isolation of infectious MCF MuLV from spleen cells of 7-wk-old mice. A role for MCF MuLV in Cas-Br-M MuLV-induced nonthymic lymphomas is indicated by these studies, and a role for recombinant MuLV in neurological disease is considered. (Author abstract) (22 Refs)

31. HELPER T CELL RESPONSE AGAINST MOLONEY LEUKEMIA VIRUS IN MICE (MEETING ABSTRACT).

Debre P, Boyer B, Levy JP
No affiliation given
Immunobiol; 159(1/2):34 1981

In previous reports we demonstrated that the level of viremia and the appearance of leukemias in mice inoculated with

Moloney leukemia virus (MLV) were under H-2 and non H-2 genetic control. Three genes within the major histocompatibility complex controlled the level of circulating virus Two of them called Rmv1 and Rmv2 appear to be located in the I region, respectively in the IA and IC-S or G region. The third gene, Rmv3 was mapped to the D end of the complex in D or T region. Further studies demonstrated that Rmv1, Rmv2 and Rmv3 function as immune response (Ir) genes regulating the level of antiviral antibodies. To study more precisely the helper T cell function, we performed experiments in culturing anti MLV spleens or lymph nodes with DNP-MLV. This system allowed us to characterize 1) the timing and specificity of antiviral immune response in mice inoculated by murine sarcome virus (MSV) or inactivated MLV, 2) the phenotype and genetic control of specific helper T cells, 3) the relationship of helper function with other components of immune response in MSV infected mice. (no Refs)

32. EXPRESSION OF MURINE LEUKEMIA VIRUSES IN THE HIGHLY LYMPHOMATOUS BXH-2 RECOMBINANT INBRED MOUSE STRAIN.

Bedigian HG, Taylor BA, Meier H
Jackson Lab., Bar Harbor, ME, 04609
J Virol; 39(2):632-640 1981

Among 12 recombinant inbred strains of mice derived from crossing two strains, C57BL/6J and C3H/HeJ, which have a low incidence of neoplastic disease, one strain (BXH-2) has been found to have a high incidence of lymphoma, of non-T-cell origin, at an early age. The BXH-2 strain carries the Fv-1b allele and spontaneously expresses a B-tropic murine leukemia virus beginning at as early as 10 days of gestation and continuing throughout their life. No significant differences in ecotropic virus titers were observed at any age tested (16 to 17 days of gestation through 7 mo), whereas xenotropic virus was first detected in lymphoid tissues of 2-mo-old mice and virus titers increased with age. Dual tropic virus(es), which induced cytopathic changes on mink lung cells, was isolated from BXH-2 lymphomatous tissues. Unlike AKR mink lung focus-forming virus (N-tropic recombinant), BXH-2 dual tropic virus is B tropic and induces cytopathic changes in mouse fibroblast cultures as well. The BXH-2 mouse provides a model system for studying the role of replication-competent viruses in spontaneously occurring leukemias of non-T-cell lineage and neurological disease. (Author abstract) (38 Refs)

33. GENETIC STUDY OF LYMPHOMA INDUCTION BY AKR MINK CELL FOCUS-INDUCING VIRUS IN AKR X NFS CROSSES.

Cloyd MW, Hartley JW, Rowe WP
Lab. Persistent Viral Diseases, NIH, Rocky Mountain Laboratories, Hamilton, MT, 59840
J Exp Med; 154(2):450-458 1981

AKR mice were crossed with NFS mice. Susceptibility to lymphoma induction by AKR-247 mink cell focus-inducing (MCF) virus was measured in AKR and NFS mice, F1, F2, and various backcrosses. AKR mice, inoculated as babys or weanlings, were totally susceptible. NFS mice were totally resistant. F1 mice were completely susceptible if inoculated as babys, and partially susceptible if inoculated as weanlings. Among backcrosses, 52% were susceptible. Among F2 mice, 75% were susceptible. Virological assays indicated that AKR-247 MCF viruses were replicated only in mice containing the endogenous AKR ecotropic virus. If one virus was absent, the other was also absent. Among virus-positive mice 37% were resistant to MCF lymphomagenesis. Apparently an additional gene was involved in the development of the lymphoma. Mice with both virus-inducing loci seemed to be more susceptible than those with only one. The presence of ecotropic virus involved the generation of MCF viruses and established permissiveness for their growth. (20 Refs)

34. GOAT LYMPHOSARCOMA FROM BOVINE LEUKEMIA VIRUS.

Olson C, Kettmann R, Burney A, Kaja R
Dept. Veterinary Science, Univ. Wisconsin-Madison, 1655 Linden Drive, Madison, WI, 53706
JNCI; 67(3):671-675 1981

A goat given inoculations of sheep lymphocytes from cultures that produced bovine leukemia virus (BLV) died 8 yr later with lymphosarcoma. The tumors were located in various lymph nodes, the mesentery, omentum, body wall, and retrobulbar tissues. The BLV had been cultured from lymphocytes during the 1st yr after the goat's infection, and persisting BLV antibodies could be demonstrated when the animal was 7.5 yr old. BLV provirus was identified by molecular hybridization in the DNA of the goat tumors at the above five locations. The tumors were similar to those found in lymphosarcoma of the adult bovine type (BLV associated). Normal goat liver, normal calf thymus, and calf-type lymphosarcoma (not BLV associated) served as negative controls. Our serologic, histologic, and molecular hybridization studies are evidence that the lymphosarcoma was induced by BLV. (Author abstract) (14 Refs)

REVIEWS AND OTHER RELATED STUDIES

35. THE CHROMOSOMES IN HEMATOLOGY.

Berger R
Laboratoire de Cytogenetique, Institut de Recherches sur les Leucemies et les Maladies du Sang, UER d'Hematologie, Hopital Sant-Louis, 2 place du Dr. Fournier, 75475 Paris Cedex 10, France
Cancer Genet Cytogenet; 4(1):69-88 1981

Chromosome studies in hematological disorders made rapid and significant advances following the introduction of banding techniques, and the most salient features of these studies are succinctly reported in this review. Considering the consistency of the chromosome anomalies first, it appears that about 50% of the acute leukemias do not present with or develop detectable karyotypic changes, which could lead to the assumption that they may play a role at any level in the development of the malignant process. More recent work seems to indicate that the normal metaphases found in the marrow by direct methods and on unstimulated blood may not have originated from leukemic cells. If clonal chromosome anomalies are to be of some significance, they ought to be nonrandom in character and that is what studies of the last few yr have shown. Thus, correlations between these chromosomal anomalies and the types of malignant proliferation have been established. Other examples of nonrandom anomalies were found in acute lymphoblastic leukemia (ALL) (deletion of the long arm of chromosome number 6; translocation t(4;11)), in chronic lymphocytic leukemia, certain myeloproliferative syndromes, and in preleukemia (the 5q- anomaly). The relationship between constitutional and acquired chromosomal anomalies (*trisomy and acute leukemia*), as well as between chromosome breakage syndromes and malignant proliferation, is discussed. Modification of the chromosome changes during the course of the disease have also contributed greatly to our better understanding of these condi-

tions; disappearance of the anomalies during remission and reappearance in relapse of acute leukemia and clonal evolution, allowing critical evaluation of the relationship between the presence of consistent nonrandom chromosome anomalies and prognosis of the disease. Finally, the practical indications for chromsome investigations in hematological disease are listed, and certain future developments are mentioned. (179 Refs)

36. LYMPHOCYTE HYBRIDOMAS IN CANCER RESEARCH: EARLY HISTORY.

Sinkovics JG
2336 North Braeswood, Houston, TX, 77030
J Med; 12(2):109-126 1981

Research conducted since the early 1960's on the fusion of murine leukemia virus-producing cells and antibody-producing plasma cells is reviewed. The tissue culture of a diploid, Rauscher virus-producing lymphoma (620) yielded tetraploid lymphoma cells, because the tumor attracted immune plasma cells in vivo and fusion between a lymphoma cell and an immune plasma cell took place in cultu re. A cell line (818) established from the fused cells continued to produced leukemia virus and a specific antibody directed to the virus. This phenomenon was reproduced in in vitro and in vivo by cocultivation, or by inoculation into mouse peritoneal cavities, of 620 lymphoma cells and normal spleen cells from leukemia virus immune mice. The preparation of monoclonal antibody-producing lymphocyte hybridomas by the fusion of murine plasmacytoma cells (P3X63-Ag8) with immune spleen cells also is described. Technical requirements for the growth of the hybridomas are summarized. The possibility that hybridoma formation occurs in lymphoproliferative disorders (eg, Burkitt's tumors and Hodgkin's disease) is discussed. The Reed-Sternberg cells of Hodgkin's disease could result from the fusion of a neoplastic mononuclear cell with a specific antibody-producing plasma cells; Sezary cells are probably T-lymphocyte hybridomas formed between neoplastic and helper T cells. (46 Refs)

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NOTICE OF CURRENT REVIEWS: CARCINOGENESIS

As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

CHEMICAL CARCINOGENESIS

1. THE GENETIC TOXICOLOGY OF ALDRIN AND DIELDRIN.
Ashwood-Smith MJ
Environmental Toxicology Res. Group, Dept. Biology, Univ. Victoria, Victoria, BC V8W 2Y2, Canada
Mutat Res; 86(2):137-154 1981

RADIATION CARCINOGENESIS

2. EFFECTS OF LOW-LEVEL RADIATION ON BIOLOGIC SYSTEMS: A LITERATURE REVIEW.
Best TL, Hoditschek B
Eastern New Mexico Univ., Portales, NM
Effects of Low-Level Radiation on Biologic Systems: A Literature Review. Available from National Technical Information Service, Springfield, VA, as SAND-80-7143:, 246 pp., 1981.

3. PHOTOCARCINOGENESIS: AN OVERVIEW.
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4. EPIDEMIOLOGICAL CORRELATIONS BETWEEN DIET AND CANCER FREQUENCY.
Correa P
Louisiana State Univ. Medical Center, New Orleans, LA, 70112
Cancer Res; 41(9,part2):3685-3689 1981

5. ROLE OF DIETARY FIBER IN DIVERTICULAR DISEASE AND COLON CANCER.
Talbot JM
Life Sciences Res. Office, Federation of American Societies for Experimental Biology, Bethesda, MD, 20014
Fed Proc; 40(9):2337-2342 1981

EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

6. PRIMARY HEPATIC CANCER IN ALCOHOLICS.
Tamburro CH, Lee HM
Liver Res. Center, Div. Digestive Diseases and Nutrition, Univ. Louisville Health Sciences Center, 511 South Floyd St., Louisville, KY, 40232
Clin Gastroenterol; 10(2):457-477 1981

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9. GENETICS OF WILMS'S TUMOR.
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Hum Genet; 57(3):231-246 1981

CELLULAR AND MOLECULAR MECHANISMS IN CARCINOGENESIS

10. NEOPLASMS: COMPARATIVE PATHOLOGY OF GROWTH IN ANIMALS, PLANTS, AND MAN.
Kaiser HE
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Neoplasms: Comparative Pathology of Growth in Animals, Plants, and Man. Baltimore, Williams and Wilkins, 908 pp., 1981.

11. PULMONARY CARCINOGENESIS: ARYL HYDROCARBON HYDROXYLASE.
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Dept. Medicine, Baylor Coll. Medicine, Houston, TX, 77030
Cancer Treat Res; 1:1-34 1981

12. THE GENETIC TOXICITY OF HYDROXYLAMINES.
Marfey P, Robinson E
Dept. Biological Sciences, State Univ. New York at Albany, Albany, NY, 12222
Mutat Res; 86(2):155-191 1981

MODIFICATION OF CARCINOGENESIS

13. MODIFYING FACTORS OF CHEMICAL CARCINOGENESIS.
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Medical Inst., Gorki, USSR
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15. PATHOGENESIS OF THYMIC LYMPHOMAS IN C57BL MICE.
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Laboratoire d'Anatomie Pathologique, Tour de Pathologie B. 23, Universite de Liege au Sart Tilman, 4000 Liege, Belgium
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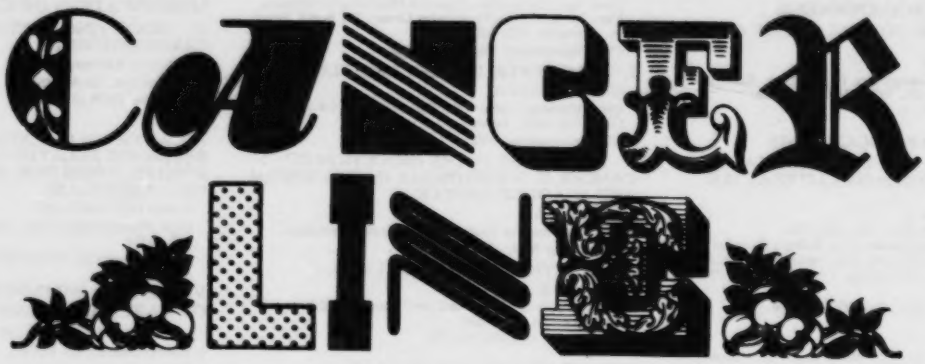
Prog Clin Biol Res 45: 327 pp., 1981.



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Lymphatic and Hematopoietic Tissues

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EPIDEMIOLOGY AND ETIOLOGY OF HUMAN LYMPHORETICULAR MALIGNANCIES: VIRAL STUDIES

1. BURKITT'S LYMPHOMA IN JAPAN: CLINICOPATHOLOGICAL FEATURES OF TWENTY-TWO PATIENTS.

Abe K, Sato T
Dept. Pediatrics, Hokkaido Univ. Sch. Medicine, Kitaku, Sapporo 060, Japan
Tohoku J Exp Med; 134(3):289-293 1981

Twenty-two cases of Burkitt's lymphoma in Japan were reviewed and their clinicopathological features were compared with those reported in African and American patients. There were 14 males, 8 females; aged 1-29 yr, mean age 9.5 yr. Most (19) were between 1 and 15 yr old. Five were Stage I, eight Stage II, six Stage III, and three Stage IV. Sites of involvement included the facial bone (20), abdomen (8), exophthalmus (5), cranial neuropathy (3), paraplegia (1), testes (1), and breast (1). The bone marrow was involved and leukemic transformation was observed in seven patients during the course of their disease. One of 17 patients tested for antibody titers to Epstein-Barr virus had a significantly elevated level. Serum lactic dehydrogenase levels were lower in patients with localized disease than those with advanced disease. The mean survival was 3.8 mo after diagnosis and no significant differences were found between the stage of disease and survival. (16 Refs)

2. INFECTION WITH EPSTEIN-BARR VIRUS AND TUMOR ORIGIN IN THE HUMAN.

Kirchner H
Deutsches Krebsforschungszentrum, Institut fur Virusforschung, D-6900 Heidelberg, W. Germany
Naturwissenschaften; 68(8):418-422 1981

The Epstein-Barr Virus (EBV) is the only infectious agent for which a close association with human malignant tumors has been clearly demonstrated. These tumors are one type of nasopharyngeal carcinoma which is frequent in parts of East Asia and the Burkitt lymphoma which predominantly occurs in parts of Africa and New Guinea. Nonetheless, the EBV is the causative agent of infectious mononucleosis (IM), a benign, self-limiting lymphoproliferative disease of adolescents. The major difference between the countries in which the EBV-induced tumors occur and those in which IM occurs is the late primary EBV infection in the latter, whereas primary infection with EBV occurs in the first yr of life in the former. All theories of viral carcinogenesis have to explain the long latency period between primary infection and tumor growth and how an ubiquitous virus may be oncogenic. Thus, invariably, one has to assume a role of cofactors, which may be of cytogenetic nature or may be represented by additional infections or by chemical agents. Since most modern theories of carcinogenesis consider a multi-step development of tumors, the theory that infection with an ubiquitous virus at the right time of life represents one step to carcinogenesis seems to be tenable. (Author abstract) (7 Refs) (In GER)

3. EPSTEIN-BARR VIRUS INFECTION AND NEOPLASIA.

Sprinkle PM, Veltri RW
Dept. Otolaryngology, West Virginia Univ., Morgantown, WV
Otolaryngol Head Neck Surg; 89(4):542-544 1981

Conclusive serological data of activation of Epstein-Barr virus (EBV) is reported showing persistently elevated early antigen (EA) titers prior to and following malignant transformation in a 6-yr-old boy. Heterophil-negative EBV disease characterized by lymphadenopathy and recurrent tonsillitis developed in the child 1 mo after his sister died with heterophil-negative infectious mononucleosis. Epstein-Barr nuclear antigen (EBNA) and EA were detected in many B-lymphocytes present in each of the same tissue specimens. One yr later, rebiopsy of the cervical nodes revealed typical Hodgkin's disease. EBNA and EA were found in hilar and celiac lymph nodes as well as in splenic lymphocytes. Serum antibody study demonstrated a 1:640 EA and 1:2,560 viral capsid antigen-IgG specific antibody to their EBV-coded antigens. Before and after the diagnosis of Hodgkin's disease, however, the patient's EA titers were persistently elevated and remained so. The child was alive with a poor prognosis after multiple chemotherapy courses and two courses of radiotherapy. The child's mother died in the interim with undifferentiated lymphoma. (16 Refs)

EPIDEMIOLOGY AND ETIOLOGY OF HUMAN LYMPHORETICULAR MALIGNANCIES: OTHER STUDIES

4. CARCINOGENICITY, MUTAGENICITY AND TERATOGENICITY OF NICKEL.

Leonard A, Gerber GB, Jacquet P
Dept. Radiation Biology, C.E.N.-S.C.K., B-2400 Mol, Belgium
Mutat Res; 87(1):1-15 1981

Nickel is widely used in the metallurgical industry. It is not released into the environment in large quantities, but poses an occupational hazard to human health. Ingested nickel is not readily absorbed, hence it is relatively nontoxic. Inhaled nickel is toxic in certain forms. Nickel carbonyl at 30 ppm for 30 min is lethal. Half-life in the body is less than 1 wk. Metallic nickel can cause sensitization of the immune system. Nickel compounds are carcinogenic in inverse proportion to their solubility in aqueous media. Nickel sulfide appears to have the greatest carcinogenicity. The lungs and nasal tissue are favored sites of nickel-induced cancers. Tumor types induced include undifferentiated sarcoma, fibrosarcoma, carcinoma, leukemia, and lymphoma. The mutagenicity of nickel is uncertain: nickel may be mutagenic in mammals but not in microorganisms. It is capable of crossing the placenta and has teratogenic effects, including fetal mortality, exencephaly, and cystic lung disease, in some species. Effects may be delayed by retarded transfer across the placenta. (129 Refs)

5. BENZENE AS A RISK FACTOR.

Stobbe H
Universitatsklinik fur Innere Medizin 'Theodor Brugsch', Bereich Medizin der Humboldt-Universitat, Schumannstrasse 20/21, DDR-1040 Berlin, E. Germany
Arch Geschwulstforsch; 51(7):575-578 1981

Exposure to benzene as a risk factor of hematological diseases is reviewed and illustrated by recent cases. The hematopoietic disorders induced by benzene are manifested usually several mo to decades after exposure and are irreversible disturbances of the hemopoietic stem cells (erythropoietic, monocytopoietic, granulocytopoietic, and thrombocytopoietic cell lines), mostly with predominance of one of these myeloproliferative cell systems. Three different clinical pictures can be

observ ed in the course of the further progression: aplastic bone marrow syndrome (aplastic anemia), hematopoietic dysplasia (preleukemia), and acute leukemia (erythroleukemia, myeloblastic, promyelocytic, or myelomonocytic forms). Transition from one clinical picture to another is also possible. Two hundred fifteen cases of disease due to benzene and its homologs were recognized in East Germany during the period 1974-1979. The analysis of 11 cases of hematological diseases due to occupational exposure to benzene showed that 4 patients were chemical workers, 5 mechanics, 1 was a painter, another an art restorer using gasoline containing benzene. The length of exposure was 0.5-45 yr. The analysis of the history of the disease in 10 cases revealed aplastic bone marrow syndrome in 6 cases (the length of exposure was 6-12 yr in 3/6); preleukemia in 6, including 3 patients who developed preleukemia after aplastic bone marrow syndrome; acute leukemia in 3 patients after exposure for 5-45 yr, and chronic myeloid leukemia in 1 patient after exposure for 9 yr. The patients with acute leukemia included one in which leukemia was preceded by preleukemia and aplastic bone marrow syndrome. (7 Refs) (In GER)

6. CANCER RISK IN PESTICIDE-EXPOSED AGRICULTURAL WORKERS.

Barthel E
Bezirksfachkrankenhaus fur Lungenkrankheiten und Tuberkulose, Amsee 1, DDR-2060 Waren (Muritz), E. Germany
Arch Geschwulstforsch; 51(7):579-585 1981

Cancer risk was studied in 1,658 agricultural workers who had been exposed to pesticides for at least 5 yr in a cohort study. Malignant tumors were found in 169/1,658 cases; the tumors were confirmed histologically in 124/169 cases. Tumors of the esophagus, nasal cavity, soft tissues, lymphoid tissue, skin melanoma, lymphosarcoma, and lymphocytic leukemia were diagnosed in 1 case each. Other tumors included stomach in 21 cases, rectum in 7, liver in 2, gallbladder in 2, pancreas in 7, larynx in 4, trachea, bronchi, and lungs in 59, skin in 19, prostate in 11, penis in 2, urinary bladder in 7, brain in 2, and thyroid gland in 2. Lymphogranulomatosis was diagnosed in two cases, plasmocytoma in three, and myeloid leukemia in two. The difference between the exposed group and general epidemiological data was significant for lung cancer only (50 cases among exposed patients from 1970-1978 versus an expected value of 27.5). The av length of exposure of the lung cancer patients was 13.6 yr (6-23 yr), and the av latent period was 17.5 yr (6-29 yr). The higher incidence was not related to smoking habits, which suggests the etiological role of pesticide exposure. Based on intraindividual exposure data, experimental data, and on the use of pesticides in East Germany, the pesticides of greatest concern are arsenic-containing compounds, dicophane (DDT), lindane, and phenoxy acids. (21 Refs) (In GER)

7. INBORN ERRORS OF TYROSINE METABOLISM IN CHILDREN WITH HEMOBLASTOSES.

Raushenbakh MO, Ivanova VD, Shevchenko VE, Makhonova LA, Sergeev AV, Baikova VN, Levchuk AA, Balakirev SA, Vares IM, Maiakova SA
All-Union Cancer Res. Center, Moscow, USSR
Vestn Akad Med Nauk SSSR; (7):19-24 1981

Various aspects of tyrosine metabolism were studied in 36 children (aged 15 days to 15 yr) with hemoblastoses and their parents. Of 36 children, 31 had acute leukemia, 3 had hematosarcoma, 1 had sympathoblastoma, and 1 had congenital histiocytosis X. Children with hemoblastoses showed a 2.3x increase of urinary excretion of tyrosine (TR), 2.3x increase of urinary excretion of p-hydroxyphenylpyruvic acid (HPPA), and 36.6x increase of urinary excretion of p-hydroxylacetic acid (HPLA). Of 36 children, 12 did not excrete homogentisic acid, while in 24 the urinary excretion of homogentisic acid (HGA) amounted to 0.95 mg/day, compared with 1.46 mg/day in healthy controls. Compared with healthy adults, the parents of children with hemoblastoses had elevated urinary excretion of TR, HPPA and HPLA. Av urinary excretion of HGA in parents was 1.23-1.94 mg/day, compared with 4.08 mg/day in healthy adults. (16 Refs) (In RUS)

8. IN VIVO AND IN VITRO ETHYLENE OXIDE EXPOSURE OF HUMAN LYMPHOCYTES ASSESSED BY CHEMICAL STIMULATION OF UNSCHEDULED DNA SYNTHESIS.

Pero RW, Widegren B, Hogstedt B, Mitelman F
Wallenberg Lab., Univ. Lund, Fack 7031, 220 07 Lund 7, Sweden
Mutat Res; 83(2):271-289 1981

Evidence of toxic exposure to ethylene oxide (EO) in factory workers producing disposable medical equipment was sought in 17 exposed women and 11 unexposed female controls from the same plant. EO exposure was 0.5-1.0 ppb for 40 hr/wk in 12 packers and 5-10 ppb for 8 hr/wk in 4 sterilizers and 1 lab technician, using the measurement of N-acetoxy-2-acetylaminofluorene (NA-AAF)-induced unscheduled DNA synthesis (UDS) in lymphocytes as the assay. The results for the controls in this study agreed with previous results for unexposed subjects: age and/or chromosome aberrations increased in a positive linear manner with increases in NA-AAF-induced UDS. However, the results for the EO-exposed packers were completely different for these two parameters: tendencies toward negative linear correlations were observed that were so divergent from controls (even for this small sample size) that these two groups were shown to be borderline significantly different populations. The data for the other group of exposed workers was nearly significantly different from that for the packers, indicating that perhaps the EO exposure in this group was not high enough to cause a significant reduction in NA-AAF-induced UDS. These results were corroborated by in vitro measurements of EO-induced (0.1-30 milliM) UDS in cultured lymphocytes: at greater than 2 milliM EO, UDS was inhibited, and even at the 0.1 milliM dose where UDS was not affected the exposed cells were sensitized to further exposure to NA-AAF, which caused a 40% cytotoxicity compared with 5% in controls. EO is toxic to lymphocytes and nontoxic doses of EO can sensitize cells to the cytotoxic action of other mutagens. (21 Refs)

9. LYMPHOMA IN THREE MEMBERS OF THE SAME FAMILY.

Spremolla G, Petrini M, Ambrogi F, Grassi B
Via di Padule, 16, 56100 Pisa, Italy
Haematologica (Pavia); 66(2):228-232 1981

Cases of three women from the same family with lymphoma, two well-differentiated lymphocytic and one Hodgkin's disease, are described. One 68-yr-old woman presented with generalized adenopathy, epigastric pain, and postprandial vomiting. Supraclavicular biopsy allowed the diagnosis of well-differentiated lymphocytic lymphoma. The patient was treated with polychemotherapy. A sister of Patient 1 had been diagnosed at the age of 41 yr as having Hodgkin's disease. Following alternate phases of remission and deterioration, and after treatment with numerous polychemotherapeutic cycles, the patient had been asymptomatic for 5 yr. A 39-yr-old niece of Patients 1 and 2 presented with multiple laterocervical and supra-

clavicular adenopathies. Supraclavicular lymph node biopsy revealed well-differentiated lymphocytic lymphoma. She was treated with a polychemotherapy regimen and remained asymptomatic. The etiology of lymphoma is discussed with respect to these three cases of lymphoma found in one family; notable aspects are the simultaneous presence of two very different types of lymphoma and concordance in the female sex. Genetic factors seem more important than infectious causes. (19 Refs)

10. ESTIMATION OF STOCHASTIC RISK FROM COMPUTED TOMOGRAPHIC EXAMINATIONS IN JAPAN, 1979. 3. ESTIMATION OF POPULATION DOSES AND STOCHASTIC RISKS.

Nishizawa K, Maruyama T, Iwata T, Furuya Y, Hashizume T
Dept. Radiology, Sch. Medicine, Kyorin Univ., 6-20-2 Shinkawa, Mitaka-shi, Tokyo 181, Japan
Nippon Igaku Hoshasen Gakkai Zasshi; 41(5):436-441 1981

The population doses and stochastic risks of hereditary leukemia and malignant diseases from computed tomographic examinations were estimated on the basis of a 1979 nationwide survey of randomly sampled hospitals and clinics throughout Japan. The organ or tissue doses related to genetic effects and somatic effects were determined with a phantom measurement, using thermoluminescent dosimeters and seven types of computed tomographic scanners. The resultant annual population doses per person were 0.11 mrad (1.1 uGy) for genetically significant dose, 2.8 mrad (28 uGy) for per caput mean bone marrow dose, 2.2 mrad (22 uGy) for leukemia significant dose and 0.72 mrad (7.2 uGy) for malignancy significant dose, respectively. Assuming that computed tomographic examinations in 1979 will be performed continuously in the future, the population risks for the whole population in Japan were estimated to be 20 persons per yr for total risks. As an example of results, the individual risks were 7.36 x 10(-6) for a 32 yr old male and 8.23 x 10(-6) for a 32 yr old female from cranial computed tomographic examinations and 101.0 x 10(-6) for a 12 yr old male and 257 x 10(-6) for a 12 yr old female from lower abdominal computed tomographic examinations. (Author abstract) (10 Refs) (In JPN)

CYTOGENETIC AND MORPHOLOGIC STUDIES

11. CHROMOSOME STUDIES IN ADULT T-CELL LEUKEMIA IN JAPAN: SIGNIFICANCE OF TRISOMY 7.

Ueshima Y, Fukuhara S, Hattori T, Uchiyama T, Takatsuki K, Uchino H
Dept. Medicine, Box 420, Univ. Chicago, Chicago, IL, 60637
Blood; 58(3):420-425 1981

Chromosomes were studied in cells from 15 Japanese patients with adult T-cell leukemia (ATL). Mitoses were obtained from unstimulated peripheral blood in 12 patients and a lymph node in 1 patient. In two other patients, mitotic cells were obtained solely from peripheral blood stimulated with phytohemagglutinin (PHA). Chromosomally abnormal cells were seen in 14 of the 15 patients. The abnormal cells had a modal number of chromosomes in near diploid range in 12 patients, and in near triploid and tetraploid range in the remaining 2 patients, respectively. Eight of the nine patients analyzed by Q-banding had clonal chromosome abnormalities. The most common abnormality was trisomy number 7 or 7q, which was seen in five cases and has been primarily observed in lymphoid neoplasms. A 14q+ marker chromosome was found in two patients and a Dq+ in one patient; loss of a sex chromosome was found in three patients. Most chromosomes were involved in gains, losses, or structural rearrangements, but abnormalities of number 11, which have been frequently found in lymphoid malignancies, was not observed in our series. The significance of these chromosome abnormalities is discussed. (Author abstract) (37 Refs)

12. CHROMOSOME ANALYSIS IN BONE MARROW LYMPHOCYTES IN CHILDREN WITH ACUTE LYMPHOCYTIC LEUKEMIA AND PRELEUKEMIA.

Karolyi G, Kosztolanyi Gy, Kajtar P, Molnar S
Gyermekklinika, Pecsi Orvostudomanyi Egyetem, Pecs, Hungary
Orv Hetil; 122(34):2087-2088,2091 1981

Chromosome analyses were carried out in bone marrow and peripheral blood lymphocytes from 19 children with acute lymphocytic leukemia, 11 children with preleukemia (including polycythemia vera and pancytopenia), and from 19 adults with chronic myeloid leukemia. The Philadelphia chromosome and chromosome 1 were affected most frequently. The heterochromatic portion of chromosome 1 was asymmetrically enlarged or reduced in some of the children with leukemia and preleukemia, and pericentric inversion was found in one case. The findings support the general assumption of a relationship between the C band and the development of malignant disease. Correlation was found between the clinical and cytogenetic picture. (11 Refs) (In HUN)

13. CHROMOSOME ABNORMALITIES IN DOWN'S SYNDROME PATIENTS WITH ACUTE LEUKEMIA.

Kaneko Y, Rowley JD, Variakojis D, Chilcote RR, Moohr JW, Patel D
Dept. Medicine, Box 420, Univ. Chicago, 950 East 59th St., Chicago, IL, 60637
Blood; 58(3):459-466 1981

Chromosome and cytologic studies were performed on three Down's syndrome (DS) patients with acute nonlymphocytic leukemia (ANLL). All three patients had an aneuploid clone in their leukemic cells: 50,XX,+6,19,+21,+22, 48,XX,+8,+21, and 47,XY,+8,-21,+dic(21:21)(p13;p11). Every patient appeared to have acute undifferentiated leukemia when the blast cells were examined with Wright-Giemsa stain; cytochemistry studies, however, showed that the leukemic blasts were in an early stage of myeloid differentiation. The two patients with +8 had a preleukemic phase; the blast cells of the patient with an extra number 19 and number 22 could not be differentiated morphologically from those of the two patients with an extra number 8. Our finding and a review of data on 40 other patients suggest that most DS children with ANLL have hyperdiploidy, which is usually related to gains of C, F, and/or G chromosomes, and that the abnormalities of +8 and of +19,+22 in DS children may be associated with acute leukemia (AL) in an early stage of myeloid differentiation. (Author abstract) (41 Refs)

BIOCHEMICAL, IMMUNOLOGICAL AND OTHER CELL BIOLOGY STUDIES

14. ULTRASTRUCTURAL, CELL MEMBRANE, AND CYTOGENETIC CHARACTERISTICS OF B-CELL LEUKEMIA, A MURINE MODEL OF CHRONIC LYMPHOCYTIC LEUKEMIA.

Slavin S, Weiss L, Morecki S, Bassat HB, Leizerowitz R, Gamliel H, Korkesh A, Voss R, Polliack A
Dept. Medicine, Immunology Res. Lab., Jerusalem, Israel
Cancer Res; 41(10):4162-4166 1981

A murine model of a spontaneous, transplantable BALB/c B-cell leukemia (BCL1) is described. Extreme leukemia and splenomegaly develop in H-2d-compatible recipients of tumor cells. Tumor cells are medium to large lymphocytes that can be transformed in plasmacytoid cells following in vitro stimulation with lipopolysaccharide. Karyotype analysis of transformed tumor cells reveals 36 chromosomes with several monosomies and 7 marker chromosomes. The ultrastructure of the tumor cells was studied using transmission and scanning electron microscopy. Although the appearance of tumor cells seems normal by morphological criteria, an impaired capping ability was documented using the fluorescein-conjugated concanavalin A-binding test. Impaired capping ability was documented before leukemia was overt as early as 1 to 3 days following inoculation of tumor cells. The B-cell leukemia (BCL1) provides a useful murine model for the study of various aspects of human bone marrow-derived malignant disorders. (Author abstra ct) (28 Refs)

15. IMMUNOPREVENTION OF FRIEND VIRUS-INDUCED ERYTHROLEUKEMIA BY VACCINATION WITH VIRAL ENVELOPE GLYCOPROTEIN COMPLEXES.

Hunsmann G, Schneider J, Schulz A
Forschergruppe Tumorimmunologie, D-7800 Freiburg, W. Germany
Virology; 113(2):602-612 1981

Adult STU mice were repeatedly immunized with aggregates of Friend virus envelope glycoprotein gp85. The antigen was given emulsified in incomplete Freund's adjuvant. After the last boost, animals were challenged with a dose of FLV inducing fatal erythroleukemia in 90-100% of the controls. Twenty of 20 mice immunized with 100 ug of gp85 were completely protected, while 3 of 7 animals vaccinated with 10 ug of gp85 died of leukemia. Smaller doses were ineffective, as was the adjuvant alone. Only animals that had developed a strong antibody response survived the FLV challenge. Serum antibodies of these animals reacted with type-, species-, and interspecies-specific determinants of pg85. Only a marginal cellular reactivity to gp85 was detected. The development of viremia was monitored by the use of radioimmunoassay for the internal viral core polypeptide p30. Animals completely protected were not viremic later than 7 days post-FLV infection. Those mice of the immunized groups which died in spite of an early antibody response showed a sharp decrease in serum antibodies to gp85 and a simultaneous appearance of virus in blood about 2-4 wk before death from leukemia. Thus, the suppression of virus spread by antibody seems to be important for immuno-prevention of this virus-induced leukemia. (Author abstract) (26 Refs)

16. CYCLIC UREA AND THIOUREA DERIVATIVES AS INDUCERS OF MURINE ERYTHROLEUKEMIA DIFFERENTIATION.

Li C, Mella SL, Sartorelli AC
Dept. Pharmacology, Comprehensive Cancer Center, Yale Univ. Sch. Medicine, New Haven, CT, 06510
J Med Chem; 24(9):1089-1092 1981

A series of derivatives of tetramethylurea, a known inducer of the differentiation of Friend erythroleukemia cells, has been synthesized and tested for its capacity to induce erythroid maturation, as measured by the synthesis of Hb. Cyclic urea and thiourea derivatives consisting of five-, six-, and seven-membered ring systems containing N-alkyl substituents were prepared. Most of these agents were relatively effective inducers of differentiation, with N-alkyl substitution appearing to be essential for max response. The most potent agents developed were N,N'-dimethyl cyclic ureas. Exposure to concentrations of 2 to 4 mM of these derivatives resulted in more than 90% of the cell population achieving a differentiated state. Under these conditions, the parent compound, tetramethylurea, was slightly less efficacious, causing differentiation of only 68% of the population at its max effective level of 4 mM. (Author abstract) (32 Refs)

EXPERIMENTAL STUDIES INVOLVING CHEMICAL AGENTS AND IRRADIATION

17. THE DETECTION OF IN VIVO HEMATOTOXICITY OF BENZENE BY IN VITRO LIQUID BONE MARROW CULTURES.

Harigaya K, Miller ME, Cronkite EP, Drew RT
(c/o Cronkite) Medical Res. Center, Brookhaven Natl. Lab., Upton, NY, 11973
Toxicol Appl Pharmacol; 60(2):346-353 1981

The hematotoxicity and possible leukemogenicity of benzene was tested. by inhalation was tested in female C57BL/6J mice. Groups of mice were exposed either to normal air or to air containing benzene (400 ppm) for 6 hr/day/5 days/wk for 9 days or 11 consecutive days. Cultures were then made from bone marrow samples. Each culture contained an adherent (A) fraction (consisting of phagocytic mononuclear cells, fat cells, endothelial cells , and epithelial cells) and a non-adherent (NA) fraction (consisting mainly of granulocytes and macrophages). The number of spleen colony-forming cells was progressively reduced in cells from benzene-treated mice. Cultures from benzene-treated mice had a reduced capacity to maintain stem cell proliferation compared to cell cultures from normal cells, as shown by combining normal or treated A fractions with various reinoculations. Evidently benzene injures stem cells, reducing their ability to self-replicate and deranging the A cell population. Neonatal C57BL/6J mice injected with cells from benzene-treated mice did not develop leukemia during 8 mo after injection. This suggests that benzene may promote, rather than initiate, leukemia. (28 Refs)

EXPERIMENTAL STUDIES: DNA TUMOR VIRUSES

18. ENHANCEMENT OF EPSTEIN-BARR VIRUS-INDUCED TRANSFORMATION OF HUMAN LYMPHOCYTES BY TELEOCIDIN.

Hoshino H, Miwa M, Fujiki H, Sugimura T, Yamamoto H, Katsuki T, Hinuma Y
Natl. Cancer Center Res. Inst., Tsukiji, Chuo-ku, Tokyo 104, Japan
Cancer Lett; 13(4):275-280 1981

The effect of teleocidin and 12-O-tetradecanoyl-phorbol-13-acetate (TPA) on Epstein-Barr virus (EBV)-induced transformation in human lymphocytes was examined. Human umbilical cord lymphocytes were infected with the B95-8 strain of EBV and cultured in soft agar. Teleocidin enhanced colony-forming efficiency approx 5x at 0.1 nanog/ml. TPA had a similar but lesser effect at the same concentration. Optimal concentrations were, respectively, 2.2 and 1.6 x 10(-10) M. Using the P3HR-1 EBV strain, which unlike strain B95-8 induces early antigen (EA) in C-6 lymphoblastoid cells after superinfection, the effects on plating efficiency were tested. The number of EA-positive cells as detected by immunofluorescence increased 2-3x in the presence of teleocidin or TPA. Cultures not infected with P3HR-1 produced less than 1% EA-positive cells even with teleocidin or TPA. Colony-forming efficiency of the newly transformed lymphoblastoid cells was 2x as great in the presence of 0.5 nanog/ml teleocidin as in its absence. TPA is known to have a similar effect. The evidence suggests that teleocidin and TPA act similarly to enhance the efficiency of EBV infection of cord blood lymphocytes and also to stimulate colony formation of lymphocytes newly transformed by EBV. (19 Refs)

19. HYBRIDIZATION OF A MOUSE T-CELL LYMPHOCYTE LINE (HB1) WITH A POLYOMA VIRUS-TRANSFORMED MOUSE FIBROBLAST LINE.

Berebbi M, Foa C, Barra Y, Simonetti J, Meyer G
Unite 119 de l'INSERM, F-13009 Marseille, France
Exp Cell Res; 134(2):445-456 1981

The establishment of permanent T-lymphocyte cell lines by transformation with DNA viruses has not yet been achieved. This paper reports the successful transfer of polyoma virus genome into T-lymphocyte cells by somatic hybridization. A T-lymphocyte clone, HB1, derived from (DBA/2J x AKR) spleen cells, isolated in vitro by cloning in semi-solid agar, was fused with a polyoma (Py) virus-transformed fibroblast (C3HPy, clone 1). The authenticity of the hybrid C3H/HB was established by chromosome and histocompatibility antigen studies. This initial population and the various clones retained T-lymphocyte characteristics such as morphological appearance, growth properties (suspension culture) and differentiation antigen (Thy 1-2). The hybrid cell line and the various clones presented all the characteristics of Py transformation. Namely, they carried the Py genome originating from the fibroblastic parent and maintained Py virus tumor-associated antigens (TSTA, TSSA and T antigens). In most respects, this hybrid population resembled the C3HPy/C11 parent and exhibited the same tumorigenicity. (Author abstract) (28 Refs)

EXPERIMENTAL STUDIES: RNA TUMOR VIRUSES

20. VIRUSES AS COFACTORS IN CHEMICAL CARCINOGENESIS.

Fey F
Zentralinstitut fur Krebsforschung, Akademie der Wissenschaften der DDR, Lindenberger Weg 80, DDR-1115 Berlin-Buch, E. Germany
Arch Geschwulstforsch; 51(7):611-614 1981

The interaction between viruses and chemical carcinogens was studied in mice. Newborn XVII mice were administered cell-free endogenous virus isolate from the thymus, lymph nodes, bone marrow, and spleen of mice with nitrosomethylurea (NMU)-induced leukemia; 1 wk later a suboptimal dose of NMU (50 ug) was given (Group I). Two control groups were treated either with the cell-free isolate (Group II) or with the suboptimal NMU dose (Group III). The animals which survived were killed after 16 mo to prevent occurrence of spontaneous leukemia. The number of animals with leukemia and tumors was 35/72 (48.6%) in Group I, 5/38 (13.2%) in Group II, and 3.31 (9.7%) in Group III. The frequency of neoplasms is significantly higher in Group I than in Groups II and III. The latent period was 388 days in Group I, 464 days in Group II, and 462 days in Group III. The findings were confirmed in a similar experiment with C57Bl x BALB/C hyb rid mice with an extremely low incidence of spontaneous leukemia: the tumor incidence was 3x higher after combined treatment with virus isolate and the carcinogen than after treatment with virus isolate and the carcinogen than after treatment with either one alone. The findings indicate the synergistic effects of viruses and chemical carcinogens in the murine system. (14 Refs) (In GER)

21. MYELOID AND ERYTHROID NEOPLASTIC RESPONSES TO AVIAN DEFECTIVE LEUKEMIA VIRUSES IN CHICKENS AND IN QUAIL.

Moscovici C, Samarut J, Gazzolo L, Moscovici MG
Tumor Virology Lab. (151), Veterans Admin. Medical Center, Gainesville, FL, 32602
Virology; 113(2):765-768 1981

A comparative study of the oncogenic potential of two avian defective leukemia viruses (DLVs) shows that avian erythroblastosis virus induces myeloid leukemia in quail and confirms that E26 causes erythroid leukemia in chickens. These results indicate that the response of birds to these two DLVs depends on the host species and suggest that classification of DLVs based only on in vitro studies may not be definitive. (Author abstract) (9 Refs)

22. PHYSICOCHEMICAL AND IMMUNOLOGICAL PROPERTIES OF TISSUE DNA FROM MICE WITH ONCORNAVIRUS-INDUCED LEUKEMIA.

Chamova KG, Perelazayi AA, Guseva NI
Res. Lab. Experimental Immunobiology, Moscow, USSR
Biull Eksp Biol Med; 91(7):60-62 1981

DNA specimens isolated from the spleen of mice with leukemia induced by Freund leukemia virus or by Rauscher virus were found to contain the antigenic determinants that were absent in the normal homologous DNA. Denaturation of leukemic DNA did not affect its immunologic specificity. (10 Refs) (In RUS)

23. ONCOGENICITY OF GIBBON RETROVIRUS DETERMINED BY LEUKEMIA-SPECIFIC GENOMIC SEQUENCES.

Sun L, Kawakami TG
(c/o Kawakami) Comparative Oncology Lab., Univ. California, Davis, CA, 95616
Virology; 114(1):261-264 1981

The genome of a Type C virus, GaLV-5, isolated from several clinically healthy gibbons, was examined for the presence of nucleotide sequences related to the myelogenous leukemia-specific 'MYE' RNA and the lymphocytic leukemia-specific 'LYM' RNA which have been isolated from several strains of oncogenic GaLV. The genomes of these oncogenic GaLVs were each separated into sequences homologous and nonhomologous to GaLV-5. Based on hybridization analysis, the nonhomologous RNA fractions were found to contain either the MYE RNA or the LYM RNA. This indicates that the leukemia-specific RNAs are lacking in the genome of GaLV-5. This lack was further confirmed by analysis of hybridization kinetics. The presence of leukemia-specific RNA sequences in GaLV genomes that were isolated from animals with leukemia and the absence of these sequences in virus strains isolated from animals free of clinical symptoms of leukemia indicate tha t the leukemia-specific RNA sequences are closely associated with the oncogenesis of leukemia in gibbons. (Author abstract) (17 Refs)

24. IMMUNOPATHOLOGY OF NATURAL AND EXPERIMENTAL LYMPHOMAS INDUCED BY WILD MOUSE LEUKEMIA VIRUS.

Bryant ML, Scott JL, Pal BK, Estes JD, Gardner MB
(c/o Gardner) Dept. Pathology, Univ. California Sch. Medicine, Davis, CA, 95616
Am J Pathol; 104(3):272-282 1981

Naturally occurring lymphomas of Lake Casitas (LC) wild mice, and the lymphomas induced by LC murine leukemia virus (MuLV) in Swiss mice from the National Institutes of Health, displayed remarkably similar gross, microscopic, and functional characteristics. They spared the thymus, arose primarily in the splenic red pulp, became leukemic, and were comprised of stem cells lacking classic T- and B-cell markers. Cytoplasmic and surface Ig were undetectable in 34 of 35 spontaneous LC lymphomas and in any of 10 LC MuLV-induced lymphomas in NIH Swiss mice. Assays for Ig secretion, complement (C'3) and Fc receptors, Thy 1.1,2 antigens, Ly 1,2 antigens, and erythroid and myeloid markers were negative on all of the spontaneous and experimental lymphomas. Cell lines were derived from five spontaneous lymphomas of LC mice. Three lines were characterized as null cells, one line as B cells, and one line as macrophages. All cell lines were diploid. The wild mouse spontaneous lymphomas, and lymphomas experimentally induced by LC MuLV in laboratory mice, provide a useful model for childhood acute lymphoblastic leukemia and for study of the early steps of B-lymphocyte differentiation. (Author abstract) (64 Refs)

REVIEWS AND OTHER RELATED STUDIES

25. BURKITT'S LYMPHOMA.

Ziegler JL
NCI, Bethesda, MD, 20205
N Engl J Med; 305(13):735-745 1981

Recent developments that have added to the understanding of biologic, etiologic, and clinical aspects of Burkitt's lymphoma (BL) are reviewed. Detailed discussions present the immunology of malignant lymphoma, and etiology, clinical features, staging, treatment, and immunology of BL. BL now ranks with the dozen neoplasms that can be cured by drugs alone. BL is also the leading candidate for a virus-induced human tumor; studies of this association led to the discovery of Epstein-Barr virus as the cause of infectious mononucleosis. Experimental and clinical examination of BL have greatly expanded the study of immunobiology and tumor immunology. (121 Refs)

26. A NEW LOOK AT MALIGNANT LYMPHOMAS.

Parker JW
Sch. Medicine, Univ. Southern California, Los Angeles, CA
Diagn Med; 4(4):77-80,85,87-90,92,94,96,98-100,103-105,108,110,113 1981

A general review is presented of malignant lymphomas (ML), the diagnosis and treatment of which has greatly improved in the last 10 yr. The classification of ML as either lymphocytic or hi stiocytic is being reconsidered today in light of our new understanding that the immune system consists of three major compartments: T and B lymphocytes, and histiocytes/macrophages and that malignant cells can arise from any of these compartments. The process and results of lymphocyte transformation in vitro have been studied extensively. B cell lymphomas develop as transformations in the follicular centers of lymphoid tissues. The genesis of T cell lymphomas is less well understood. Both T and B cells have immunoregulatory functions that may be retained by neoplastic lymphoid cells. Many immunological, functional, and cytochemical markers are useful for distinguishing T cells, B cells, and histiocytes; combinations of these markers also distinguish lymphoma/leukemia cells. Cytochemical and histochemical procedures can be used to identify leukemias and lymphomas, although no one stain or enzyme is totally specific for a given neoplastic cell type. Immunohistochemistry and immunocytochemistry have become useful in diagnosis, particularly techniques using antibodies conjugated with enzymes. The application of these methods and concepts to the differentiation of lymphomas and leukemias is discussed. Lymphocytic lymphomas are neoplasms of the immune system that may represent cells that are blocked in certain stages of their normal development or transformation. (22 Refs)

27. RADIOACTIVITY IN DRINKING WATER.

Cothern CR
Office of Drinking Water, Environmental Protection Agency, Washington, DC
Radioactivity in Drinking Water. Available from National Technical Information Service, Springfield, VA, as PB81-192833:, 79 pp., 1981.

This general overview is designed to assist those involved with public health and drinking water to better understand, interpret and implement EPA's regulation for radioactivity in drinking water. In this presentation the general nuclear properties are shown using naturally occurring .sotopes such as

radium, radon and uranium as examples. The units of radio-activity (curie, rad and rem) are explained and demonstrated in describing natural radiation; in our surroundings and bodies as well as man-made radiation from medical x-rays, TV, fallout, industrial uses and nuclear power plants and other sources. The health effects discussed include birth defects, genetic damage, cancers, leukemias and others. Several specific examples are given in each disease area as well as their relative importance or rate of occurrence. The risk (in deaths/million people exposed/yr) is tabulated for radioactivity and compared to several other cases including disease, accidents and weather. Possible methods for reducing the radioactivity in drinking water are described. Flow charts are provided that show how to interpret the radiation regulations for drinking water. (Author abstract)

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NOTICE OF CURRENT REVIEWS: CARCINOGENESIS

As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

CHEMICAL CARCINOGENESIS

1. TOXICOLOGICAL ASPECTS OF POLYCYCLIC AROMATIC HYDROCARBONS (PAH).
De Fernicola NA, De Azevedo FA
Divisao de Toxicologia e Ecotoxicologia, Diretoria de Tecnologia e Desenvolvimento, Sao Paulo, Brazil
Rev Bras Saude Ocup; 33(9):62-68 1981
In POR

2. EVALUATION OF THE CARCINOGENIC RISK OF CHEMICALS TO HUMANS: SOME ANTINEOPLASTIC AND IMMUNOSUPPRESSIVE AGENTS.
International Agency for Research on Cancer
International Agency for Res. on Cancer, Lyon, France
IARC Monogr Eval Carcinog Risk Chem Hum; 26:1-411 1981

3. STUDIES ON THE ROLE OF ORAL CONTRACEPTIVE USE IN THE ETIOLOGY OF BENIGN AND MALIGNANT LIVER TUMORS.
Mettlin C, Natarajan N
Cancer Control and Epidemiology, Rosewell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
J Surg Oncol; 18(1):73-85 1981

RADIATION CARCINOGENESIS

4. EXPERIMENTAL RADIATION CARCINOGENESIS: WHAT HAVE WE LEARNED?
Fry RJ
Biology Div., Oak Ridge Natl. Lab., Oak Ridge, TN, 37830
Radiat Res; 87(2):224-239 1981

5. INFLUENCE OF NONCARCINOGENIC SECONDARY FACTORS ON RADIATION CARCINOGENESIS.
Little JB
Lab. Radiobiology, Harvard Univ., Sch. Public Health, Boston, MA, 02115
Radiat Res; 87(2):240-250 1981

6. MEDICAL IRRADIATION IN JAPAN - STOCHASTIC RISK ESTIMATION AND ITS REDUCTION.
Hashizume T
Div. Physics, National Inst. Radiological Sciences, 9-1 Anagawa 4-Chome, Chiba Shi 260, Japan
Nippon Igaku Hoshasen Gakkai Zasshi; 41(5):445-474 1981
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7. RADIOACTIVITY IN DRINKING WATER.
Cothern CR
Office of Drinking Water, Environmental Protection Agency, Washington, DC
Radioactivity in Drinking Water. Available from National Technical Information Service, Springfield, VA, as PB81-192833:, 79 pp., 1981.

EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

8. EPIDEMIOLOGY OF GASTROINTESTINAL CANCER.
Miller AB
NCIC Epidemiology Unit, Univ. Toronto, McMarrich Building, Toronto, Ontario M5S 1A8, Canada
Compr Ther; 7(8):53-58 1981

9. EPIDEMIOLOGICAL ASPECTS OF ESOPHAGEAL CANCER.
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IV Cattedra di Clinica Chirurgica Generale e Terapia Chirurgica, Universita degli Studi di Roma, Rome, Italy
Recenti Prog Med; 70(5):545-556 1981
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10. PANCREATIC CANCER.
Cohn I, Hastings PR
Dept. Surgery, Louisiana State Univ., 1542 Tulane Ave., New Orleans, LA, 70112
UICC Tech Rep Ser. Vol. 57, Issue 12, 142 pp., 1981.

11. GENETICALLY DETERMINED SUSCEPTIBILITY TO CANCER.
Marks PA
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Blood; 58(3):415-419 1981

12. ETIOLOGY, ROLE AND DETECTION OF CHROMOSOMAL ABERRATIONS IN MAN.
Fabricant JD, Legator MS
Dept. Preventive Medicine, Div. Environmental Toxicology, Univ. Texas Medical Branch, Galveston, TX, 77550
JOM; 23(9):617-625 1981

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13. INDUSTRIAL CARCINOGENESIS.
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14. ENVIRONMENT AND HEALTH (LITERATURE REVIEW).
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Dept. Public Health, State Inst. Advanced Training for Physicians, Erevan, USSR
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15. LIFESTYLE AND CANCER.
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Cancer Forum; 5(1):4-14 1981

16. ASBESTOS, AN ENVIRONMENTAL POLLUTANT.
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Institutul de igiena si sanatate publica, Iasi, Romania
Igiena; 30(1):1-9 1981
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Gray N
Smoking and Cancer Program, UICC, 3 rue du Conseil General, 1205 Geneva, Switzerland
Cancer Forum; 5(1):15-18 1981

CELLULAR AND MOLECULAR MECHANISMS IN CARCINOGENESIS

18. EXPERIMENTAL APPROACHES TOWARDS THE BIOCHEMICAL ANALYSIS OF CHEMICAL CARCINOGENESIS.
Laishes BA
McArdle Lab. for Cancer Res., Univ. Wisconsin Medical Sch., Madison, WI, 53706
ACS Symp Ser; 160:197-215 1981

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ICRDB Program Office, NCI, Westwood Building, Room 10A18, Bethesda, MD, 20205
Preneoplastic Lesions of the Mammary Gland (Oncology Overview) Medina, D, ed This Title is Available Through National Technical Information Service, Springfield, VA, as NTISUB/PB81-923002; OB-81/02:134pp. 1981

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Magrath IT
Pediatric Oncology Branch, Div. Cancer Treatment, NCI, NIH, Public Health Service, United States Dept. Health and Human Services, Bethesda, MD, 20205
JNCI; 67(3):501-514 1981

MODIFICATION OF CARCINOGENESIS

22. FACTORS STIMULATING AND INHIBITING TUMOR GROWTH IN CARCINOGENESIS.
Kochergina NI, Kosova IP
Res. Lab. Experimental Immunobiology, Moscow, USSR
Usp Sovrem Biol; 91(3):409-418 1981
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23. TWO INDEPENDENT ASPECTS OF TUMOR PROMOTION.
Berenblum I, Armuth V
Weizmann Inst. Science, Rehovot, Israel
Biochim Biophys Acta; 651(1):51-63 1981

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Weinberg RA, Steffen DL
Center for Cancer Res., Massachusetts Inst. Technology, Cambridge, MA, 02139
J Gen Virol; 54(part1):1-8 1981

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Durkin PR, Santodonato J
Center for Chemical Hazard Assessment, Syracuse Res. Corporation, Merill Lane, Syracuse, NY, 13210
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Short-Term Test Systems for Potential Mutagens and Carcinogens: I Microbial Tests (Oncology Overview) Simmon, V F; Peirce, V; eds This Title is Available Through National Technical Information Service, Springfield, VA, as NTISUB/PB81-922903:; OK-81/03:124pp. 1981

28. ANIMAL MODELS OF INTRA-ORAL CHEMICAL CARCINOGENESIS: A REVIEW.
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Dept. Oral Medicine and Pathology, Guy's Hosp., London SE1 9RT, England
J Oral Pathol; 10(3):129-146 1981

29. THE CHROMOSOMES IN HEMATOLOGY.
Berger R
Laboratoire de Cytogenetique, Institut de Recherches sur les Leucemies et les Maladies du Sang, UER d'Hematologie, Hopital Sant-Louis, 2 place du Dr. Fournier, 75475 Paris Cedex 10, France
Cancer Genet Cytogenet; 4(1):69-88 1981

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Lymphatic and Hematopoietic Tissues

SERIES CK20 No. 82/03

MARCH, 1982

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

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EPIDEMIOLOGY AND ETIOLOGY OF HUMAN LYMPHORETICULAR MALIGNANCIES: VIRAL STUDIES

1. SUMMARY: SYMPOSIUM ON EPSTEIN-BARR VIRUS-INDUCED LYMPHOPROLIFERATIVE DISEASES IN IMMUNODEFICIENT PATIENTS.

Klein G, Purtilo D
Dept. Tumor Biology, Karolinska Institutet, S-104 01 Stockholm 60, Sweden
Cancer Res; 41(11,part1):4302-4304 1981

The possibility that the X-linked lymphoproliferative syndrome, renal transplant lymphomas, and other lymphomas in immunodeficient patients originate in proliferating Epstein-Barr virus (EBV)-carrying lymphoid cells is discussed. Evidence for this association included the detection of EBV nuclear antigen (EBNA) in virus-transformed cells and changes in EBV antibody titers in immunodeficiency conditions. Defects of the T-cell system were associated with increased titers against EBV early and viral capsid antigens and decreased anti-EBNA titers. Chronic infectious mononucleosis patients and X-linked lymphoproliferative syndrome patients showed marked impairment of all effector mechanisms involved in the rejection of EBV-carrying cells. (23 Refs)

2. SEROEPIDEMIOLOGIC STUDIES IN HODGKIN'S DISEASE.

Kokosha LV, Lapin BA, Lebedev VN, Danilova NV, Arshba NN, Bologov VN
Lab. Experimental Oncology, Inst. Experimental Pathology and Therapy, Sukhumi, USSR
Probl Gematol Pereliv Krovi; 26(8):12-16 1981

To evaluate the possibility of horizontal transmission of Epstein-Barr virus (EBV), antibodies against capsid antigen of EBV were determined in 109 patients with Hodgkin's disease (HD) and in 67 relatives of 46 patients. High titers of antivirus antibodies were recorded in 70% of the patients with HD. The highest titers were recorded in the patients with lymphoid exhaustion (1:256, compared with 1:97 in lymphoid predominance and mixed cell variant, and 1:49 in nodular sclerosis). The titers of antibodies against EBV antigen in the relatives were significantly greater that that in healthy donors (1:69 and 1:6, respectively). (34 Refs) (In RUS)

3. INFECTIOUS MONONUCLEOSIS AND ACUTE LEUKEMIA.

Rosner F, Grunwald HW
Dept. Medicine, Long Island Jewish-Hillside Medical Center, 82-68 164 St., Jamaica, NY, 11432
JAMA; 246(16):1783-1784 1981

Relationship between infectious mononucleosis and acute leukemia is discussed with respect to 26 reported cases in which the diseases coexisted. No clear relationship was found between Epstein-Barr virus, infectious mononucleosis, and acute leukemia; future cell typing of forms of acute leukemia other than Burkitt's lymphoma may allow detection of subtypes with distinct Epstein-Barr virus receptors, providing some possible linkage between the development of leukemia and that of infectious mononucleosis. (21 Refs)

EPIDEMIOLOGY AND ETIOLOGY OF HUMAN LYMPHORETICULAR MALIGNANCIES: OTHER STUDIES

4. IMPLICATIONS OF NEW HIROSHIMA AND NAGASAKI DOSE ESTIMATES: CANCER RISKS AND NEUTRON RBE.

Straume T, Dobson RL
Hazards Control Dept., Lawrence Livermore Natl. Lab. Box 808, Livermore, CA, 94550
Health Phys; 41(4):666-671 1981

Dose-response relations for radiation-induced leukemia, breast cancer, total malignancies, and chromosome aberrations in atomic bomb survivors were analyzed with the use of new dose esti mates that differ substantially from the generally accepted values. They indicate that the gamma ray component and total dose were higher in Hiroshima than previously believed and lower in Nagasaki; neutron components were lower in both cities. Dose-response curves for leukemia and breast cancer were similar in the two cities, but those for total malignancies and chromosome aberrations demonstrated significant inter-city differences. The inter-city differences were due to an increase in neutron relative biological effectiveness (RBE) with decreasing dose due to diminished gamma-ray effectiveness. The neutron RBE for leukemia and breast cancer induction remain to be clarified. (13 Refs)

5. A HYPOTHESIS ON THE ETIOLOGY OF ADULT T-CELL LEUKEMIA/LYMPHOMA.

Tajima K, Tominaga S, Shimizu H, Suchi T
Div. Epidemiology, Aichi Cancer Center Res. Inst., 81-1159 Kanokoden, Tashiro-cho, Chikusa-ku, Nagoya 464, Japan
Gan; 72(5):684-691 1981

The results of the nationwide survey performed by the T- and B-cell Malignancy Study Group revealed that adult T-cell leukemia/lymphoma (ATLL) was prevalent in limited zones in Kyushu, mainly in coastal areas, warm in winter and humid in summer. It was found that the geographical distribution of filariasis was very similar to that of ATLL. It is known that filariasis affects lymphatic vessels and results in several lymphoreticular ailments, and microfilaria is transmitted by mosquitoes infected with some kinds of not yet fully identified viruses. From analyses of the time trends of the av wt and height of school children by prefecture, it is suggested that the nutritional condition of inhabitants in Kyushu might have been poorer than that of inhabitants of other areas in Japan, especially in the past. In order to elucidate the etiology of ATLL, relevant geographic-pathological information and other related information was accumulated and an etiological hypothesis was formulated. It was hypothesized that repeated exposure to filarial antigen and some viruses might have played an important role in the etiology of ATLL and that undernutrition had also contributed to the progression of ATLL. (Author abstract) (31 Refs)

6. PHENOXY ACIDS, CHLOROPHENOLS, AND CANCER.

Hardell L, Eriksson M
Onkologiska kliniken, Regionsjukhuset, Umea, Sweden
Lakartidningen; 78(34):2862-2863 1981

Recent studies on the carcinogenic effects of phenoxy acids and chlorophenols in occupationally exposed subjects are reviewed. Relationship between exposure to phenoxy acids and

chlorophenols and malignant mesenchymal soft-tissue tumors was found in two case-control studies in Sweden. Increased risk of malignant lymphoma was also demonstrated in another study. Malignant lymphoma, acute leukemia, and malignant mesenchymal soft-tissue tumors were found at significantly increased incidence a mong workers exposed to (2,4,5-trichlorophenoxy)acetic acid 2,4,5-trichlorophenol, and the impurity 2,3,7,8-tetrachloro-dibenzo-p-dioxin (TCDD). TCDD was found to induce malignant mesenchymal soft-tissue tumors, and 2,4,6-trichlorophenol caused increased incidence of hepatocellular carcinoma, malignant lymphoma, and leukemia in rats. (15 Refs) (In SWE)

7. BENZENE INDUCED BONE-MARROW INSUFFICIENCY.

Haak HL
Dept. Hematology, Municipal Hosp. 'Leyenburg', Leyweg 275, 2545 CH The Hague, The Netherlands
Trends Pharmacol Sci; 2(10):265-267 1981

History, clinical and experimental findings, and cytogenetic effects of benzene are discussed in relation to benzene-induced bone marrow insufficiency. A high level of benzene exposure has been associated with high incidence of pancytopenias and bone marrow dysplasia. A small number of these cases may develop into leukemia, usually of the acute myelogenous variety. The overall incidence of malignant disease in highly exposed individuals is approx double that of the general population. The risk of lower levels of exposure is a matter of epidemiological debate. Experimental studies indicate that benzene induces hematopoietic failure at the level of the maturing progenitor cell, beyond the pluripotent stem cells. Such failure is expressed by progressive dysplastic changes in bone marrow and peripheral blood. In addition, several lines of investigation have indicated a deranged interaction between stem cells, progenitor cells, and the regulating microenvironment. Unlike the situation in humans, no malignancy has been induced by benzene in vivo in animals. Perhaps in humans additional toxicity is afflicted on the hematopoietic stem cell. (10 Refs)

EPIDEMIOLOGY AND ETIOLOGY OF NON-HUMAN LEUKEMIA AND LYMPHOMA

8. FELINE LEUKEMIA VIRUS NONPRODUCER LYMPHOSARCOMAS OF CATS AS A MODEL FOR THE ETIOLOGY OF HUMAN LEUKEMIAS.

Hardy WD, McClelland AJ, Zuckerman EE, Snyder HW, MacEwen EG, Francis D, Essex M
No affiliation given
Haematol Blood Transfus; 26:492-494 1981

Immunological and epidemiological studies of feline lymphosarcoma (LSA) are summarized. Immunofluorescent antibody assay, immunodiffusion, tissue culture isolation, and radioimmunoassay were used to test 507 casts with LSA for feline leukemia virus (FeLV). FeLV-positive LSA was found in 360 cats; the remaining 147 had nonproducer (NP) LSA. No FeLV proteins or infectious viruses were detected in NP LSA. However, the FeLV-induced tumor specific oncovirus-associated cell membrane antigen was detected on the surface of both NP and FeLV positive LSA cells. Of 1,612 FeLV-exposed and -unexposed cats observed for development of LSA, 0/1,074 unexposed cats (observed av 3 yr/cat) developed LSA; 149/538 exposed cats (observed av 4.4 yr/cat) were persistently infected. LSA developed in 41 cats, 30 FeLV positive and 11 NP LSA. Difference in rate of NP LSA in FeLV-exposed and -unexposed cats was significant (p less than 0.001). FeLV appears to be the etiologic agent of feline LSA regardless of FeLV status. Mechanisms by which RNA- and DNA-containing viruses induce tumors are discussed. Feline NP LSA could be a useful model for elucidating mechanisms of oncovirus transformation. (12 Refs)

CYTOGENETIC AND MORPHOLOGIC STUDIES

9. THE IMPLICATIONS OF NONRANDOM CHROMOSOME CHANGES FOR MALIGNANT TRANSFORMATION.

Rowley JD
Dept. Medicine, Section Hematology/Oncology., Box 420, 950 East 59th St., Chicago, IL, 60637
Haematol Blood Transfus; 26:151-155 1981

How and why chromosome changes occur are discussed in relation to malignant transformation. The mechanism for the production of specific, consistent, reciprocal translocations is unknown. A clear difference in preferential break points for chromosome translocations, was observed depending on whether the rearrangement resulted in a balanced or an unbalanced aberration. Other possible explanations depend on either chromosomal proximity, since translocations may occur more frequently when two chromosomes are close together, or regions of homologous DNA that might pair preferentially and then be involved in rearrangements. Kinds of gene loci that can provide a proliferative advantage during nonrandom changes are considered including the host genome and chromosome changes related to gene dosage (homogeneously staining regions and double minute chromosomes and evidence for gene amplification). (28 Refs)

10. CHROMOSOME STUDIES IN CHILDREN AND ADULTS WITH LEUKEMIA.

Rowley JD
Dept. Medicine, Section Hematology/Oncology, Box 420, 950 East 59th St., Chicago, IL
Haematol Blood Transfus; 26:27-33 1981

Chromosome abnormalities are described in various myeloid leukemias including Philadelphia chromosome (Ph1)-positive myelogenous leukemia (chronic and acute), acute nonlymphocytic leukemia, and acute lymphoblastic leukemia. Within each category, the data that have been collected are correlated with clinical information. The identification of nonrandom chromosome changes in these various myeloproliferative and lymphoproliferative disorders are reviewed. Although the data available for these disorders are quite variable both with regard to the number of patients studied and the quality of banding, patterns of chromosome changes can be discerned that differ among the various groups. Wherever possible these pattern were related to structural and functional characteristics of these cells as determined by others as well as to the clinical correlations of particular chromosome changes. (26 Refs)

11. CHROMOSOMAL ABNORMALITIES IN ACUTE LYMPHOBLASTIC LEUKEMIA: STRUCTURAL AND NUMERICAL CHANGES IN 234 CASES.

Mitelman F
(c/o A. Sandberg), Roswell Park Memorial Inst., Buffalo, NY, 14263
Cancer Genet Cytogenet; 4(2):101-110 1981

Chromosomal abnormalities were found in cultured bone marrow and blood cells from 218/330 untreated patients and 16 treated patients with acute lymphoblastic leukemia. Five children and two adults (2.1% of the patients) had constitutional abnormalities, as opposed to 0.73% of 3,993 recently surveyed newborn infants. Of the 234 abnormal clones, 119 were pseudodiploid, 86 hyperdiploid, and 29 hypodiploid. Structural changes occurred in 204 cases, either alone (103) or combined with numerical changes (101); numerical changes alone accounted for 30 cases. The most common structural change was the presence of the Philadelphia chromosome associated with a translocation to chromosome 9. Chromosomes 1, 4, 6, 8, 11, and 14 also were involved in the structural changes. Lymphocyte marker studies in 182 cases showed that 72% were null cells, 19% T cells, and 9% B cells. Philadelphia chromosome-positive patients and those in the hyperdiploid category were all classified as having null cell leukemia. (8 Refs)

12. DIRECT CYTOGENETIC STUDIES BY NEEDLE ASPIRATION OF BURKITT'S LYMPHOMA IN GHANA, WEST AFRICA.

Biggar RJ, Lee EC, Nkrumah FK, Whang-Peng J
Environmental Epidemiology Branch, Div. Cancer Cause and Prevention, NCI, NIH, US Dept. of Health and Human Services, Bethesda, MD, 20205
JNCI; 67(4):769-776 1981

With the use of a needle aspiration technique for obtaining tumor material, the direct karyotype of Burkitt's lymphoma cells was examined from 14 Ghanaian patients. The 14q+ chromosome (in addition to other chromosomal abnormalities) was present in 8 (57%) of the 14 patients; 6 of these 8 patients had t(8;14) (q24;q32). One of the remaining two patients had a 8 chromosome deleted, whereas the second had two normal-appearing 8 chromosomes. Other numerical and structural abnormalities were frequent. No correlation between type or frequency of abnormality and clinical status or survival was found. Within cells of the same tumor aspirate, the karyotype abnormalities were generally similar. In three patients, karyotypes from two separate tumor sites (abdomen-bone marrow, 2 cases; right maxilla-left mandible, 1 case) showed identical markers. The same marker was seen in specimens from the initial and second relapse abdominal tumors of one patient. The similarity of chromosomal markers from two sites or in serial studies further supports the concept that African Burkitt's lymphoma is a disease of monoclonal origin. (Author abstract) (19 Refs)

BIOCHEMICAL, IMMUNOLOGICAL AND OTHER CELL BIOLOGY STUDIES

13. NORMAL AND LEUKEMIC GRANULOPOIESIS.

Gavosto F, Aglietta M
I Cattedra di Patologia Medica, Universita degli Studi di Torino, Corso Polonia, 14, 10126 Torino, Italy
Haematologica (Pavia); 66(1):1-17 1981

This editorial reviews current understanding of the development of normal and le ukemic cells. The supply of normal blood cells must be continuously replenished. This is accomplished by the totipotential stem cell, described as a colony-forming-unit-spleen because it forms splenic colonies in irradiated animals. Strong cytogenetic and enzymatic evidence suggests that myeloid leukemias represent monoclonal expansion of a single transformed cell; in chronic form, the transforming event probably affects a pluripotent stem cell. Whether this occurs in acute myelocytic leukemia, or instead primary transformation occurs in the granulocyte-oriented cell is not certain. Granulopoiesis represents the most altered differentiative line; growth models and response to regulation factors of granulocyte-monocyte-oriented stem cells have been studied to learn about prognosis and pathogenesis of uncontrolled leukemic proliferation. Recent experiments by the authors suggest that prostaglandins might be important in granulo-monocytopoiesis. Insensitivity to prostaglandins may be one of the main causes of uncontrolled leukemic proliferation. (71 Refs) (In ITA)

14. INDUCTION OF ARYLHYDROCARBON HYDROXYLASE AND BLAST TRANSFORMATION IN HUMAN BLOOD LYMPHOCYTES.

Fukuhara M, Bohuon C, Gharbi N, Biret F, Boudene C
Inst. Public Health, Shirokanedai, Minoto-ku, Tokyo, 108, Japan
Biochem Biophys Res Commun; 102(1):8-14 1981

The induction of arylhydrocarbon hydroxylase (AHH) by benzo(a)pyrene and the degree of blast transformation were measured simultaneously in peripheral hyman lymphocytes. While the induction ratio (induced:basal level) of AHH and induction ratio per unit of blast transformation varied at different culture times and at different phytohemagglutinin (PHA) concentrations for a particular individual, the ratio of absolute induced AHH activity and unit of blast transformation yielded a consistent value at different culture times and different PHA concentrations for the individual. AHH inducibility may be a useful parameter for the study of cancer susceptibility if inducibility is expressed in this new manner. (23 Refs)

15. LY 11.2: A CELL SURFACE ANTIGEN THAT MAY IDENTIFY MURINE LYMPHOCYTES SUSCEPTIBLE TO TRANSFORMATION BY ONCOGENIC AGENTS.

Meruelo D, Paolino A, Flieger N, Offer M, Dworkin J
Irvington House Inst., Dept. Pathology, New York Univ. Medical Center, New York, NY, 10016
Fed Proc; 40(12):2717-2720 1981

Ly 11.2, a newly defined T cell surface antigen, is present on two lymphocyte subpopulations playing a key role during leukemogenesis: the natural killer cell and possibly the target cells for malignant transformation by oncogenic agents. Antibodies to this cell surface marker should greatly help in the study, isolation, and characterization of these cells. (Author abstract) (20 Refs)

16. ON THE RELATION OF CROHN'S DISEASE TO LYMPHOMA PRODUCTION IN ATHYMIC MICE (MEETI NG ABSTRACT).

Das KM, Valenzuela I, Williams SE, Baum S
Albert Einstein College of Medicine, Bronx, NY
Gastroenterology; 80(5,part2):1132 1981

B cell lymphoma developed in athymic nude (nu/nu) mice following injection of Crohn's disease (CD) filtrates. We have obtained additional lymphomas (5) and hyperplastic lymph nodes (HLN) (5) in nude mice after injecting filtrates from 4 other CD patients. One hundred twenty-one coded sera from

92 patients were used to examine antigenic recognition of lymphomas and HLN by indirect immunofluorescence (IFA). Serum was absorbed with uninjected nu/nu mouse spleen cells and serum protein. Eighty percent of sera in symptomatic DC and 19% of sera in asymptomatic DC had positive cytoplasmic IFA against at least 3 lymphomas. Sera in active CD had 60% positive IFA against HLN. In contrast, no serum from patients with ulcerative colitis or control subjects showed IFA to lymphomas or HLN. Two control mice developed lymphomas. These lymphomas did not show IFA with CD or control sera. Electron microscopic examinations revealed C-type viral particles in 5 lymphomas induced by CD filtrates and in one control lymphoma but not in 5 HLN and 5 other control lymph nodes. These studies suggest that an 'antigen(s)' in CD tissue stimulates the lymphoid system of nu/nu mice resulting in hyperplasia and lymphoma either directly or by activation of murine virus. Sera from patients with symptomatic CD recognize an antigen(s) in the lymphomas induced by CD filtrates but not in control lymphomas. CD sera also recognize antigen(s) in the hyperplastic lymph nodes which did not contain C-type virus particles. (no Refs)

EXPERIMENTAL STUDIES INVOLVING CHEMICAL AGENTS AND IRRADIATION

17. CARCINOGENICITY OF BENZYL CHLORIDE, BENZAL CHLORIDE, BENZOTRICHLORIDE AND BENZOYL CHLORIDE IN MICE BY SKIN APPLICATION.

Fukuda K, Matsushita H, Sakabe H, Takemoto K
Dept. Experimental Toxicology, Natl. Inst. Industrial Health, Nagao 6-21-1, Tama-ku, Kawasaki 213, Japan
Gan; 72(5):655-664 1981

The carcinogenicity of benzyl chloride (BYC), benzal chloride (BAC), benzotrichloride (BTC) and benzoyl chloride (BOC), which were suspected as causative agents of lung cancer and maxillary malignant lymphoma of workers employed in factories producing BOC, was examined by skin applications in female ICR mice. After rather high dose exposure, BTC exhibited leukemogenic and pulmonary tumorigenic activities as well as potent dermal carcinogenic activity. After administration of the chemicals at the dose of 2.3 ul/animal, twice a wk for 50 wk, BTC induced 68% incidence of skin cancers and 58% incidence of pulmonary tumors (including 10% of lung carcinomas) within 399 days. Incidence of skin cancers was 58% for BAC, 15% for BYC and 10% for BOC within 560 days. Considering the extent of possible exposure of the workers to t hese chemicals in the working environment and the carcinogenic potency of the chemicals tested, it can be concluded that BTC was very probably responsible for causing the cancers seen in the workers employed in manufacturing BOC. (Author abstract) (16 Refs)

18. PHENOXY ACIDS: A BRIEF REVIEW OF THE POSSIBLE HYGIENIC EFFECTS.

Edling C
Yrkesmedicinska kliniken, Regionsjukhuset, Linkoping, Sweden
Lakartidningen; 78(34):2861-2862 1981

Recent studies on the hygienic effects of phenoxy acids used as pesticides are reviewed. 2,3,7,8-Tetrachloro-dibenzo-p-dioxin, occurring in a small amount as impurity in (2,4,5-trichlorophenoxy)acetic acid (2,4,5-T), was found to be a carcinogen and possibly a promotor in experimental animals. Small quantities of other dioxins, eg, tetrachloro-p-dioxin, were found in (2,4-dichlorophenoxy)acetic acid (2,4-D). Increased incidence of tumors and malformations due to 2,4,5-T was found in mice, and increased incidence of lymphosarcoma and tumors of endocrine organs was found in rats treated with 2,4-D. The mutagenicity tests of the phenoxy acids and dioxins yielded contradictory results. No carcinogenic effect of 2,4-D and 2,4,5-T was demonstrated in some animal experiments. Epidemiological studies showed a link between soft-tissue sarcoma and lymphosarcoma and exposure to phenoxy acids. Other epidemiological studies showed no relationship. Yet, a link between cancer and exposure to 2,4,5-T seems to exist in the light of experimental and epidemiological data. (10 Refs) (In SWE)

EXPERIMENTAL STUDIES: RNA TUMOR VIRUSES

19. GENETICS OF LEUKEMOGENESIS BY AVIAN LEUKOSIS VIRUSES.

Coffin JM, Tsichlis PN, Robinson HL
Dept. Molecular Biology, Tufts Univ., 136 Harrison Ave., Boston, MA, 02111
Haematol Blood Transfus; 26:432-438 1981

Biological differences between endogenous and exogenous viruses of chickens were explored in order to obtain information regarding the roles of various portions of the exogenous virus genome in pathogenicity, particularly in lymphoid leukosis. When genomes of various endogenous and exogenous viruses were subjected to T1 oligonucleotide mapping, it was concluded that these viruses represent two distinct but closely related lineages. The greatest diversity is in the U3 region near the 3' end of the genome. Studies were performed to determine the roles of various regions in regard to growth and pathogenicity of the viruses, using a series of recombinants between RAV-0 and either Pr-B or its td derivative. Repeated selection of the U3cx allele suggested responsibility for difference in growth rate between endogenous and exogenous viruses. Further studies with either endogenous or recombinant viruses indicated that the U3cx region is the major determinant responsible for the more rapid growth of exogenous viruses. A discussion is pres ented of the role of the U3 region in leukemogenesis, which clearly indicates the separation of growth rate from leukemogenicity. It is suggested that the nonpathogenicity of endogenous viruses is an adaptation to their quiescent lifestyle, which involves lack of harm to the host. The experiments described should be useful in identifying and characterizing the region of the virus genomes relevant to this adaptation and exploiting differences in various viruses in order to probe molecular mechanisms of viral leukemogenesis. (27 Refs)

20. THE MOLECULAR BASIS OF AVIAN RETROVIRUS-INDUCED LEUKEMOGENESIS.

Kung HJ, Fung YK, Crittenden LC, Fadly A, Dube SK
No affiliation given
Haematol Blood Transfus; 26:445-451 1981

The fate of proviral DNA in lymphoid leukosis (LL) induced by avian leukosis virus RAV-1 was studied. Sixteen newborn 151-5 x 7-2 chickens were each infected with 10(5) clone-purified viruses. Bursal specimens were obtained at 4 and 8 wk post infection. Leukosis appeared at 16-20 wk. DNA

from preleukosis bursae, tumors, and metastases was analyzed using complementary DNA (cDNA) and restriction endonucleases SacI and EcoRI. Three tumor-specific (TS) bands were identified in gel electrophoresis. TS bands were not present in 4-wk bursal samples, although RAV-1 fragments were, indicating that proviral DNA was integrated into host genome at multiple sites. Samples taken at 8 wk showed greater viral infection. Tumor DNA analysis indicated that only a small number of infected cells produced tumor, and that tumor origin was clonal. Variations in TS bands suggested that integration of proviral DNA at a number of sites could produce tumorigenesis. Deletions from viral genome in tumor DNA were apparent. Preferred integration sites for tumorigenesis were indicated. Metastases showed the same clonal origin as primary tumors. Multiple metastases were derived from the same clonal source, suggesting that only one of several original tumor foci contributed to secondary spread. (14 Refs)

21. STUDIES OF THE ASSOCIATION OF LEUKEMOGENIC AND ONCOGENIC PROPERTIES IN AVIAN LEUKEMIA VIRUSES.

Loliger HC, Von dem Hagen D, Hartmann W
Institut fur Kleintierzucht, Dornbergstrasse 25-27, D-3100 Celle, W. Germany
Haematol Blood Transfus; 26:452-454 1981

Induction of leukocytic and nonleukocytic neoplasias by avian myeloblastosis virus (AMV) and Marek's disease herpes virus (MDHV) was studied in chickens of Leghorn line R (cell types c/O, c/A, and c/AB), Leghorn line M (cell types c/O and c/AB), Leghorn line G (cell type c/B), dysgammaglobulinemic line UM (cell type c/O), and SPAFAS line (cell type c/O). AMV produced leukemia and nephroblastomas in all lines with homozygous cell types c/A, c/B, and c/O, but not c/AB. MDHV induced lymphoid cell reticulosis, but no leukosis, nephroblastomas, or osteosarcomas. Pretumorous lesions of the kidney appeared in 3-wk-old chickens; gross lesions with clinical symptoms appeared between 56 and 112 days after infection, with most appearing after 70 days. Osteopetrosis and osteosarcomas occurred most often in M, UM, and SPAFAS lines. AMV infection was evident in susceptible R, M, and G chickens within 2-5 wk of infection. UM chickens showed aplastic anemia with medullar fibrosis at 12-15 days, followed by stem cell leukemia. SPAFAS chickens showed erythroblastosis first, followed by stem cell leukemia and later by nephroblastomas. The more intense the early hemoblastic disorder was, the lower the chance of development of nonleukocytic neoplasms. (5 Refs)

22. DEMONSTRATION OF A SYNCARCINOGENIC EFFECT OF ENDOGENOUS MULV, RESCUED FROM MNU-INDUCED LEUKEMIAS, AND SUBOPTIMAL MNU DOSES IN MICE.

Fey F, Ehm I, Drescher B, Rentz E, Seidel G
Acad. Sciences of GDR, Central Inst. Cancer Res., 1115 Berlin, E. Germany
Neoplasma; 28(3):265-269 1981

It was demonstrated that the combined action of activated endogenous MuLV isolated from MNU-induced leukemias and suboptimal doses of MNU yields a significantly high incidence of leukemias and tumors. Treatment with one agent alone shows low effects only. The findings were discussed in view of the mechanisms in which viruses and chemical carcinogens interact in a syncarcinogenic process. (Author abstract) (11 Refs)

23. GENETIC APPROACHES TOWARD ELUCIDATING THE MECHANISMS OF TYPE-C VIRUS-INDUCED LEUKEMIA.

Aaronson SA, Barbacid M, Dunn CY, Reddy EP
Lab. RNA Tumor Viruses, NCI, Bethesda, MD, 20014
Haematol Blood Transfus; 26:455-459 1981

The mechanisms of induction of leukemia by murine type-C viruses was studied in newborn NIH/Swiss mice. Inoculations of 5 x 10(4) XC pock forming units of either Rauscher (R) or Moloney (M) murine leukemia virus (MuLV) produced gross enlargement of spleen and lymph nodes as early as 10-11 wk. RMuLV produced spleen enlargement and sometimes liver and peripheral or visceral lymph node enlargement. MMuLV produced thymus enlargement in most animals, and frequently affected other lymphoid organs. MMuLV-induced tumors were of T cell origin, as indicated by presence of Thy1 antigen and absence of Fc or C3 receptors. RMuLV-induced tumors were of B cell lineage, as indicated by presence of Fc receptors and absence of Thy1 antigen. Recombinant forms between oncogenic and nononcogenic type-C viruses were produced in wild mouse embryo cells of line WM-C. These recombinants contained genetic information in varying amounts from both parental viruses and exhibited varying degrees of oncogenicity. Results indicate that target cells for transformation by RMuLV and MMuLV contain specific markers distinguishing them from other lymphoid elements. The necessity of active virus replication for tumorigenesis by murine type-C viruses is suggested. (19 R efs)

24. CHROMOSOMAL ALTERATIONS IN THE COURSE OF VIRAL LEUKEMOGENESIS IN THE RAT.

Vernole P, Neri G, Neri ME, Serra A
(c/o G. Neri) Istituto di Genetica Umana, Universita Cattolica S. Cuore, Via Pineta Sacchetti, 644, I-00168 Roma, Italy
Cancer Genet Cytogenet; 4(2):143-155 1981

A cytogenetic study of 35 primary thymic lymphomas induced in rats by the Gross leukemia virus revealed the presence of widespread aneuploidies, ranging from cells with 35 chromosomes or less to triploid and tetraploid cells. Analysis by G banding revealed that chromosomes No 1, 2, 9, 12, 18-20, X in females, and Y in males were lost preferentially; unidentified marker chromosomes of various morphology and length were present in a high percentage of aneuploid mitoses. Similar alterations were observed in preleukemic thymi from rats sacrificed 30 days after virus injection, when clinical or histologic signs of the disease had not yet appeared. In rats that were sacrificed 7 or 15 days after virus injection, chromosomal anomalics were much more limited, although significantly more abundant than in the controls. Rats that were free of tumor at 130-160 days after virus injection showed a regression of the chromosomal anomalies, suggesting that these are not irreversible and are not necessarily followed by the development of a lymphoma. (Author abstract) (31 Refs)

25. DETERMINANTS OF SUSCEPTIBILITY AND RESISTANCE TO FELINE LEUKEMIA VIRUS INFECTION. I. ROLE OF MACROPHAGES.

Hoover EA, Rojko JL, Wilson PL, Olsen RG
Dept. Veterinary Pathobiology, Ohio State Univ., 1925 Coffey Rd., Columbus, OH, 43210
JNCI; 67(4):889-898 1981

The role of autochthonous peritoneal feline macrophages (Mtheta) in the age-related resistance of cats to feline leukemia

virus (FeLV) was investigated by a study of the functional properties and FeLV susceptibility of Mtheta from kittens and adult cats and the effect of hydrocortisone (HC) and silica on Mtheta-FeLV interactions. Although the phagocytic functions of isolated Mtheta from kittens and adults were equivalent, the mean FeLV susceptibility of Mtheta from kittens was 5x that of Mtheta from adult cats, thus establishing a direct correlation between the age-related susceptibility of cats and Mtheta from cats to FeLV. Mtheta of viremic cats were found to be infected with FeLV in vivo; virus titers were slightly higher than those obtained after in vitro infection of Mtheta. Mtheta from cats that had experienced regressive FeLV infection were not significantly more resistant to FeLV infection in vitro than were Mtheta from naive adult specific-pathogen-free cats. HC, which has been shown to enhance the in vivo FeLV susceptibility of cats, also enhanced the permissiveness of Mtheta from cats to FeLV in vitro (600-fold for Mtheta from adult cats and 200-fold for Mtheta) from kittens. Mtheta permissiveness to FeLV was highly sensitive to HC and occurred in Mtheta infected in vivo or in vitro. In parallel with the effect of HC on the natural resistance of cats to FeLV, administration of silica before virus inoculation also markedly enhanced the FeLV susceptibility of adult cats. Silica was toxic for isolated Mtheta but not for lymphocytes in vitro, and silica produced monocytopenia and neutrophilia, delayed skin allograft rejection, and augmented feline oncovirus-associated cell membrane antigen antibody responses in vivo. These experiments indicate that Mtheta were linked to the natural resistance of cats to FeLV and that the temporary elimination of Mtheta functions (eg, by silica) and/or the conversion of the Mtheta-FeLV relationship from a nonpermissive to a permissive state (eg, by corticosteroids) resulted in failure of early virus containment, in persistent virus amplification in hemolymphatic tissues, and in subsequent FeLV-related proliferative or antiproliferative disease. (Author abstract) (72 Refs)

26. DETERMINANTS OF SUSCEPTIBILITY AND RESISTANCE TO FELINE LEUKEMIA VIRUS INFECTION. II. SUSCEPTIBILITY OF FELINE LYMPHOCYTES TO PRODUCTIVE FELINE LEUKEMIA VIRUS INFECTION.

Rojko JL, Hoover EA, Finn BL, Olsen RG
Dept. Veterinary Pathobiology, Ohio State Univ., 1925 Coffey Road, Columbus, OH, 43210
JNCI; 67(4):899-910 1981

The interplay between feline leukemia virus (FeLV) and feline lymphocytes (lc) infected in vitro or in vivo was investigated. Surface marker analysis and viral infectivity (VI) assays of lc populations were used to determine susceptibility of lc subsets to FeLV. The principal FeLV-replicating cell in the mesenteric lymph node of persistently infected, preleukemic cats was a nonadherent, complement receptor (CR)-bearing lc (B-cell). The lymph nodes of preleukemic cats also had increased numbers of uninfected T-cells [cells forming rosettes with guinea pig RBC (GPE)] and cells with receptors for the Fc portion of 7S IgG (FcgammaR cells) as compared with lymph nodes of age-matched specific-pathogen-free (SPF) cats. The induction of productive infection of feline peripheral blood mononuclear WBC (PBL) in vitro depended on a 48-hr in vitro preincubation period before virus exposure. The equivalent susceptibility of whole and adherent cell-depleted PBL to productive infection and the failure of hydrocortisone to enhance viral infection were compatible with identification of the FeLV-replicating cell as an lc. Furthermore, lc from susceptible SPF kittens replicated 50x as much FeLV as did lc from resistant adult SPF cats. The lc productively infected with FeLV after in vitro exposure were more precisely identified with the use of Ficoll-Isopaque density gradient separation of rosetted and non-rosetted lc. Whole PBL, GPE rosette-positive PBL (T-cells), and CR-positive PBL (B-cells) were permissive to FeLV infection, and max VI was evident at 14 days after expos ure. The substantial (1,325-fold) increment in VI found in the FcgammaR-depleted PBL suggested a role for FcgammaR cells in the containment of FeLV infection. Unstimulated mononuclear WBC from blood, spleen, lymph node, thymus, and marrow were susceptible to productive FeLV infection after in vitro exposure. The degree of spontaneous DNA synthesis in marrow, thymus, and spleen but not lymph node or PBL was inversely related to permissiveness to viral replication. Mitogen activation of lc was associated with decreased viral replication when either T-cell mitogens (concanavalin A, phytohemagglutinin, or pokeweed mitogen) or a B-cell mitogen (dextran sulfate) was used. Virus production by spleen cells and PBL was enhanced twofold to 10-fold by prior lc stimulation by the B-cell mitogen, lipopolysaccharide, or protein A-bearing Staphylococcus aureus, a mitogen for feline T-cells with FcgammaR. Both productively infected (preincubated) and nonproductively infected (freshly isolated) PBL transferred infectious FeLV to autochthonous peritoneal macrophages (Mtheta); most of the virus in PBL-peritoneal Mtheta cocultures was produced by adherent cells, irrespective of whether the adherent or nonadherent cell population was inoculated originally. (Author abstract) (49 Refs)

27. INDUCTION OF LYMPHOSARCOMA IN SHEEP BY BOVINE LEUKEMIA VIRUS.

Kenyon SJ, Ferrer JF, McFeely RA, Graves DC
(c/o Ferrer) Sch. Veterinary Medicine, Univ. Pennsylvania, New Bolton Center, Kennett Square, PA, 19348
JNCI; 67(5):1157-1163 1981

Newborn sheep inoculated with phytohemagglutinin (PHA)-treated short-term cultures of lymphocytes from cattle infected with bovine leukemia virus (BLV) or with a BLV-infected long-term culture of bovine leukemic lymphocytes became persistently infected with BLV. Fifty percent or more of the sheep died with histologically confirmed lymphosarcomas. Cytogenetic studies of representative cases demonstrated that the tumors did not result from the progressive growth of neoplastic lymphocytes in the inoculum but rather from the neoplastic transformation of the recipient's lymphoid cells. Neither BLV infection nor lymphosarcoma was observed in control uninoculated sheep or in sheep given injections of PHA-treated cultures of lymphocytes from BLV-free cows. The virus recovered from the tumorous sheep was indistinguishable from BLV morphologically, antigenically, and biologically, and its reverse transcriptase had the same cation preference and immunologic properties as the BLV enzyme. Persistent BLV infection and lymphosarcoma were also observed in a group of sheep inoculated neonatally with BLV-containing cell-free culture supernatants. These results extend previous observations on the high susceptibility of sheep to BLV infection and provide definitive evidence that BLV is a tumor-inducing virus. (Author abstract) (33 Re fs)

28. CELLULAR TRANSFORMATION BY BOVINE LEUKEMIA VIRUS (MEETING ABSTRACT).

Amborski GF, Shane BS, Parker S, Butler D
Department of Veterinary Science, Louisiana State University, Baton Rouge, LA, 70803
In Vitro; 17(3):216 1981

Bovine leukemia virus (BLV) transformed cell lines as judged by morphological appearance, growth in reduced serum concentrations and foci formation in soft agar. Infected fetal lamb kidney cells (FLK-BLV) demonstrated foci in monolayer cultures and growth curves showed cellular multiplication in media supplemented with 2, 5 and 10% serum but not with 1%. Less than 1% of the cells grew as colonies in soft agar. Infected bat lung cells (BtLu-BLV) had less discrete foci in monolayer culture, showed similar growth patterns to FLK-BLV with varying serum concentrations but over 90% of the cells grew in soft agar. Although BtLu-BLV cells appeared more highly transformed, the amount of 3H-virus produced by both cell lines appeared similar. The exposure of both cell lines to a mutagen (5-iodo-2-deoxyuridine) did not appear to change the growth patterns in soft agar, but the level of BLV produced by both cell lines increased. (no Refs)

29. GENOMIC INTEGRATION OF BOVINE LEUKEMIA PROVIRUS AND LACK OF VIRAL RNA EXPRESSION IN THE TARGET CELLS OF CATTLE WITH DIFFERENT RESPONSES TO BLV INFECTION.

Kettmann R, Marbaix G, Mammerickx M, Burny A
Faculte des Sciences Agronomiques de l'Etat, Chaire de Zootechnie, Gembloux, Belgium
Haematol Blood Transfus; 26:495-497 1981

Bovine leukemia virus (BLV) integration sites in DNA preparations from target tissues of BLV-infected animals and viral RNA expression in the same cells were examined. DNA was digested by bacterial restriction endonucleases and submitted to electrophoresis in agarose gels. After transfer to nitrocellulose paper the DNA fragments were annealed to a specific BLV (32 P) cyclic DNA probe. Genomic DNA fragments containing viral information appeared after autoradiographic development as individual bands and sometimes smears. Comparison of BLV provirus integration and viral RNA expression in WBC of asymptomatic BLV carriers (AB+), from animals in persistent lymphocytosis (PL+), and from tumor cases (T+) was made. No BLV proviral sequences were detected in three AB+ cases. Circulating ABC of PL animals appear to accommodate BLV at many possible sites; lymphocytes infected by BLV and found in enzootic bovine leukosis tumors from two animals seemed to constitute monoclonal populations of cells carrying one copy of the proviral genome integrated at one genomic site. Liquid hybridization and BLV (3H) cyclic DNA were used to search for viral RNA sequences in total RNA samples from BLV-infected cell. In 7/8 animals tested, transcription of the integrated viral genome from WBC did not occur or occurred at a low level (5.8-8.6% hybridization). Tumor cells g ave similar results. (3 Refs)

REVIEWS AND OTHER RELATED STUDIES

30. THE RELATIVE ROLE OF VIRAL TRANSFORMATION AND SPECIFIC CYTOGENETIC CHANGES IN THE DEVELOPMENT OF MURINE AND HUMAN LYMPHOMAS.

Klein G
Dept. Tumor Biology, Karolinska Institutet, 104 Stockholm 60, Sweden
Haematol Blood Transfus; 26:3-10 1981

Lymphoma and leukemia development in mice and men, where there is extensive evidence for the role of the specific genetic changes recognizable at the chromosome level, is discussed. Topics considered include human lymphomas, murine T cell leukemia, the relationship of trisomy to murine T-cell leukemia, and the role of Abelson virus as a transducer or cellular gene. Various conclusions were drawn: transformation in vitro is not synonymous with tumorigenicity in vivo; host cell controls can modify the expression of transformation in vivo; and host cell controls can reverse tumorigenic to nontumorigenic phenotypes. The concept of convergence is discussed in relation to tumor evolution. According to this concept viruses play essentially the role of initiators in tumor progression, specific genetic changes are responsible for the transition of preneoplastic to frankly malignant cells, and the cytogenetic changes act by shifting the balance between genes that favor progressive growth in vivo and genes that counteract it. (85 Refs)

31. THE NETWORK CONCEPT AND LEUKEMIA.

Eichmann K
Krebsforschungszentrum - Immunologie, Im Neuenheimer Feld 280, 6900 Heidelberg, W. Germany
Haematol Blood Transfus; 26:343-344 1981

Application of the network concept to leukemia is discussed. Network regulation may represent a major mechanism for maintenance of steady state in the immune system. The immune system can be viewed as a series of idiotypic and anti-idiotypic compartments that regulate one another; regulation is determined by effector functions of antigen-specific elements in each compartment. Relevance to leukemia is noted: (1) unbalances in network control make certain lymphocytes susceptible to neoplastic transformation (eg the Balb/c mouse myelomas with antiphosphorylcholine specificity and T15 idiotype), and (2) specific immune therapy could involve recovery of normal T cells from leukemia patients and restimulation in vitro with leukemic cells from the same patient (restimulation methods would seek a high proportion of cytotoxic T cells with specificity for idiotypic determinants on the leukemic cells). The network concept reveals nonspecific manipulation of the immune system to be worthless; only antigen-specific measures could be expected to disturb the balance toward generation of desired effector functions. (3 Refs)

32. CURRENT STATE OF LEUKEMIA PROBLEM.

Gavrilov OK, Shishkov VP, Khokhlova MP
Central Inst. Hematology and Blood Transfusion, Moscow, USSR
Klin Med (Mosk); 59(8):6-10 1981

Current research in the field of etiology, diagnosis, treatment, and prevention of leukemia is reviewed. It was shown that leukemic transformation is associated with an increase in the level of DNA damage, inhibition of messenger RNA synthesis and transport, and inhibition of protein synthesis. In

vitro cloning of hematopoietic stem cells in semisolid agar media showed heterogeneity of the group of undifferentiated leukemias. Immunologic methods based on detection of antibodies against bovine leukemia virus showed the presence of oncornavirus infection in the cattle. Development of new antileukemia agents (hexaphosphamide, paphencil, and fotrin) and immunotherapy with viable allogeneic leukemic cells increased duration of survival of children with acute leukemia. (25 Refs) (In RUS)

* U.S. GOVERNMENT PRINTING OFFICE: 1982—361-557/112

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NOTICE OF CURRENT REVIEWS: CARCINOGENESIS

As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

CHEMICAL CARCINOGENESIS

1. CHEMICAL COMPOUNDS AND CANCER RISK.

Schramm T, Janisch W
Zentralinstitut fur Krebsforschung der Akademie der Wissenschaften der DDR, Lindenberger Weg 80, DDR-1115 Berlin, E. Germany
Arch Geschwulstforsch; 51(7):561-565 1981
In GER

2. THE CARCINOGENICITY OF ARSENIC.

Pershagen G
Dept. Environmental Hygeine, Karolinska Inst., Stockholm, Sweden
Environ Health Perspect; 40:93-100 1981

3. THE CARCINOGENICITY OF CHROMIUM.

Norseth T
Inst. Occupational Health, Gydas vei 8, Oslo 3, Norway
Environ Health Perspect; 40:121-130 1981

4. ROLE OF COBALT, IRON, LEAD, MANGANESE, MERCURY, PLATINUM, SELENIUM, AND TITANIUM IN CARCINOGENESIS.

Kazantzis G
TUC Centenary Inst. Occupational Health, London Sch. Hygiene and Tropical Medicine, Keppel St., London WC1E 7HT, England
Environ Health Perspect; 40:143-161 1981

5. RECENT RESEARCH ON NICKEL CARCINOGENESIS.

Sunderman FW
Dept. Lab. Medicine, Univ. Connecticut Sch. Medicine, Farmington, CT, 06032
Environ Health Perspect; 40:131-141 1981

6. ROLE OF CADMIUM IN CARCINOGENESIS WITH SPECIAL REFERENCE TO CANCER OF THE PROSTATE.

Piscator M
Dept. Environmental Hygiene, Karolinska Inst., S-104 01 Stockholm, Sweden
Environ Health Perspect; 40:107-120 1981

7. CHELATING AGENTS IN BIOLOGICAL SYSTEMS.

Schubert J
Dept. Chemistry, Univ. Maryland Baltimore County, Catonsville, MD, 21228
Environ Health Perspect; 40:227-232 1981

8. BENZENE AS A RISK FACTOR.

Stobbe H
Universitatsklinik fur Innere Medizin 'Theodor Brugsch', Bereich Medizin der Humboldt-Universitat, Schumannstrasse 20/21, DDR-1040 Berlin, E. Germany
Arch Geschwulstforsch; 51(7):575-578 1981
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9. FORMALDEHYDE IN DENTISTRY: A REVIEW OF MUTAGENIC AND CARCINOGENIC POTENTIAL.

Lewis BB, Chestner SB
800-A Fifth Ave., Suite 503, New York, NY, 10021
J Am Dent Assoc; 103(3):429-434 1981

10. CARCINOGENICITY OF HYDANTOINS: DATA, HYPOTHESES, AND PUBLIC REVIEWS.

Scoville B, White BG
Natl. Inst. Neurological and Communicative Disorders and Stroke, NIH, Bethesda, MD, 20205
Psychopharmacol Bull; 17(3):195-197 1981

11. PHENOXY ACIDS, CHLOROPHENOLS, AND CANCER.

Hardell L, Eriksson M
Onkologiska kliniken, Regionsjukhuset, Umea, Sweden
Lakartidningen; 78(34):2862-2863 1981
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12. PHENOXY ACIDS: A BRIEF REVIEW OF THE POSSIBLE HYGIENIC EFFECTS.

Edling C
Yrkesmedicinska kliniken, Regionsjukhuset, Linkoping, Sweden
Lakartidningen; 78(34):2861-2862 1981
In SWE

DIETARY FACTORS IN CARCINOGENESIS

13. NUTRITIONAL MODULATION OF CANCER.

Nauss KM, Newberne PM
Dept. Nutrition and Food Science, Massachusetts Inst. Technology, Cambridge, MA, 02139
Cancer Detect Prev; 3(2):367-417 1981

14. FIBER CARCINOGENESIS: EPIDEMIOLOGIC OBSERVATIONS AND THE STANTON HYPOTHESIS.

Harington JS
Cancer Res. Dept., Natl. Cancer Assoc. South Africa, P.O. Box 2000, Johannesburg 2000, South Africa
JNCI; 67(5):977-989 1981

EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

15. EPIDEMIOLOGY.

Alderson MR
Dept. Epidemiology, Inst. Cancer Res., London, England
Recent Results Cancer Res; 78:1-19 1981

16. ATLAS OF CANCER MORTALITY IN THE PEOPLE'S REPUBLIC OF CHINA. AN AID FOR CANCER CONTROL AND RESEARCH.

Li JY, Liu BQ, Li GY, Chen ZJ, Sun XD, Rong SD
Dept. Cancer Epidemiology, Cancer Inst. Chinese Acad. Medical Sciences, 2, Yabao Lu, Chaoyang, Qu, Beijing, People's Republic of China
Int J Epidemiol; 10(2):127-133 1981

ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN CARCINOGENESIS

17. SIXTH EAST GERMAN CANCER CONGRESS WITH INTERNATIONAL PARTICIPATION, BERLIN, MARCH 2-5, 1981.

Schramm T, Ebeling K, Schwarz R, Heise E, Glaser A, Tanneberger St, Anger G
No affiliation given
Arch Geschwulstforsch; 51(7):551-560 1981
In GER

18. EPIDEMIOLOGICAL STUDIES INTO THE POSSIBLE CARCINOGENICITY OF HAIR DYES.

Clemmesen J
(c/o P. Lohman), Medical Biological Lab. TNO., P.O. Box 45, 2280 AA Rijswijk, The Netherlands
Mutat Res; 87(1):65-79 1981

CELLULAR AND MOLECULAR MECHANISMS IN CARCINOGENESIS

19. THE ROLE OF METALS IN CARCINOGENESIS: BIOCHEMISTRY AND METABOLISM.

Jennette KW
Dept. Chemistry, Dartmouth Coll., Hanover, NH, 03755
Environ Health Perspect; 40:233-252 1981

20. RECENT CONCEPTS OF INITIATION AND PROMOTION IN CARCINOGENESIS.

Becker FF
M. D. Anderson Hosp. and Tumor Inst., 6723 Bertner Ave., Houston, TX, 77030
Am J Pathol; 105(1):3-9 1981

21. ACTIVATED METABOLITES OF CARCINOGENIC HYDROCARBONS.

Harvey RG
Ben May Lab., Univ. Chicago, Chicago, IL, 60637
Acc Chem Res; 14(7):218-226 1981

22. RELATIONSHIP BETWEEN METAL TOXICITY TO SUBCELLULAR SYSTEMS AND THE CARCINOGENIC RESPONSE

Squibb KS, Fowler BA
Lab. Pharmacology, Natl. Inst. Environmental Health Sciences, P.O. Box 12233, Research Triangle Park, NC, 27709
Environ Health Perspect; 40:181-188 1981

23. ENZYMES INVOLVED IN THE REPAIR OF DAMAGED DNA.

Grossman L
Dept. Biochemistry, Sch. Hygiene and Public Health, Johns Hopkins Univ., 615 N. Wolfe St., Baltimore, MD, 21205
Arch Biochem Biophys; 211(2):511-522 1981

24. METAL-INDUCED INFIDELITY OF DNA SYNTHESIS.

Zakour RA, Kunkel TA, Loeb LA
Joseph Gottstein Memorial Cancer Res. Lab., Dept. Pathol., Univ. Washington, Seattle, WA, 98195
Environ Health Perspect; 40:197-205 1981

25. CHROMOSOME ABERRATIONS AND THEIR RELEVANCE TO METAL CARCINOGENESIS.

Vainio H, Sorsa M
Dept. Industrial Hygiene and Toxicology, Inst. Occupational Health, Haartmaninkatu 1, SF-00290 Helsinki 29, Finland
Environ Health Perspect; 40:173-180 1981

MODIFICATION OF CARCINOGENESIS

26. METAL INTERACTIONS IN CARCINOGENESIS: ENHANCEMENT, INHIBITION.

Nordberg GF, Andersen O
Dept. Environmental Hygiene, Umea Univ., Umea, Sweden
Environ Health Perspect; 40:65-81 1981

27. EFFECT OF METALS ON MUTAGENESIS AND DNA REPAIR.

Rossman TG
Inst. Environmental Medicine, New York Univ. Sch. Medicine, 550 First Ave., New York, NY, 10016
Environ Health Perspect; 40:189-195 1981

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28. SISTER CHROMATID EXCHANGES: A REPORT OF THE GENE-TOX PROGRAM.

Latt SA, Allen J, Bloom SE, Carrano A, Falke E, Kram D, Schneider E, Schreck R, Tice R, Whitfield B, Wolff S
Harvard Medical Sch., Boston, MA, 02115
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29. EFFECTS OF METALS IN IN VITRO BIOASSAYS.

Sirover MA
Dept. Pharmacology, Temple Univ. Sch. Medicine, Philadelphia, PA, 19140
Environ Health Perspect; 40:163-172 1981

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EPIDEMIOLOGY AND ETIOLOGY OF HUMAN LYMPHORETICULAR MALIGNANCIES: VIRAL STUDIES

1. CLUES TO PATHOGENESIS OF EPSTEIN-BARR VIRUS-INDUCED DISEASES FROM ANALYSIS OF 100 CASES OF X-LINKED LYMPHOPROLIFERATIVE SYNDROME (XLP) (MEETING ABSTRACT).

Purtilo D, Sakamoto K, Barnabei V, Seeley J
No affiliation given
Tenth International Symposium for Comparative Research on Leukemia and Related D iseases, August 31-September 4, 1981, Los Angeles, California. 187 pp., 1981.

Comprehensive analysis of 100 cases in the Registry of XLP revealed four major phenotypes after Epstein-Barr virus (EBV) infection: 1) infectious mononucleosis (IM) including 42 fatal cases without coexisting phenotypes and 32 with other phenotypes; 2) all 18 cases of aplastic anemia occurred with IM or malignant lymphoma (ML) and never did aplastic anemia occur simultaneously with agammaglobulinemia; 3) 32 cases of ML (B cell types only) including 16 cases solely and 16 with IM; and 4) agammaglobulinemia affected 16 boys, usually with IM or ML. Rarely, 3 phenotypes occurred simultaneously. Males have profound T and B cell and natural killer cell immune defects to EBV. Several carrier females exhibit IgA and IgM anti-viral capsid antigen and anti-early antigen indicating persistent infection due to their partial immunodeficiency of XLP. Our molecular hybridization studies of tissues of seven XLP patients reveal EBV genome in all cases. Approaches to diagnosis of XLP and related disorders and rationale bases for therapy are developing as a result of these studies. (no Refs)

2. IMMUNOLOGICAL DEFECT IN A FAMILY WITH MULTIPLE NASOPHARYNGEAL CARCINOMA AND BURKITTS' LYMPHOMA (MEETING ABSTRACT).

Joncas J, Seeley J, Purtilo D, Ghibu FM, Lichaa H, Robillard L, Rioux E
No affiliation given
Tenth International Symposium for Comparative Research on Leukemia and Related Diseases, August 31-September 4, 1981, Los Angeles, California. 187 pp., 1981.

A Canadian family of 15 members, 3 of whom died of nasopharyngeal carcinoma and Burkitt's lymphoma, was investigated for immunological defects. The diagnosis made during the life of these patients was confirmed in retrospect by examination of the pathological slides by three different pathologists. A presumptive association with the Epstein-Barr virus (EBV) was supported by very high EBV antibody titers on stored sera from these patients. All the family members were EBV antibody (VCA, viral capsid antigen and EBNA, nuclear antigen) positive but EA (early antigen) antibody negative except the patients with tumors (titers up to 320) and the mother (titer of 10). The occurrence of a plasmacytoma in a maternal first degree cousin and low serum IgA values in another first degree cousin and two of the family members prompted us to follow-up this family and investigate its members further immunologically. The mother who had normal Ig levels in 1975 now has marked hypogammaglobulinemia (IgG 98 mg% and IgM 21 mg%) and has a relatively much higher EBV-VCA antibody titer than any other members of the family. The living family members except 3 male members have abnormally high numbers of T4 (helper) lymphocytes. These and other findings as well as the characteristics of the cell lines established from members of this family suggest a primary B ce ll dysfunction. The anomaly noted in T cell subpopulations is possibly secondary to the B cell dysfunction but may contribute to B cell proliferation and neoplastic transformation eventually. (1 Ref)

3. DEFECTIVE LYMPHOCYTE FUNCTION IN X-LINKED LYMPHOPROLIFERATIVE SYNDROME (MEETING ABSTRACT).

Seeley J, Lindsten T, Ballow M, Sakamoto K, Purtilo D
No affiliation given
Tenth International Symposium for Comparative Research on Leukemia and Related Diseases, August 31-September 4, 1981, Los Angeles, California. 187 pp., 1981.

Young males affected with X-linked Lymphoproliferative Syndrome (XLP) are susceptible to life-threatening Epstein-Barr virus (EBV) infections. Two-thirds of the 100 males thus far identified succumbed to fatal infectious mononucleosis (IM) while those who survived IM have developed aplastic anemia, hypogammaglobulinemia and/or B-cell lymphomas. It has been previously reported that 10 out of 12 males tested had defective Natural Killer (NK) activity. Preliminary results with the single-cell NK assay suggest a defect both in the number of target-binding XLP lymphocytes and in the lytic ability of those which do form conjugates. Although these boys have a normal numbers and percentages of peripheral T lymphocytes, their in vitro proliferative response to T mitogens is low compared to controls. Preliminary studies with cells from a hypoglobulinemia XLP male reveal reduced ability to secrete immunoglobulins in vitro in response to pokeweed mitogen (PWM). This may be an in vitro manifestation of the observation that four XLP males, immunized with a unique antigen, responded with IgM, but made no switch to IgG. (1 Ref)

4. GROWTH OF HUMAN NORMAL AND LEUKEMIC T CELLS: T-CELL GROWTH FACTOR (TCGF) AND THE ISOLATION OF A NEW CLASS OF RNA TUMOR VIRUSES (HTLV).

Gallo RC, De The, Lajtha L, Van Bekkum DW, McCulloch EA, Greaves MJ, Seligmann M, Brecher G, Shohet SB, Bessis M, Sachs L
Lab. Tumor Cell Biology, NCI, NIH, Bethesda, MD, 20205
Blood Cells; 7(2):313-329 1981

Previous studies have indicated that T-cell growth factor (TCGF) is the physiological growth promoter in the immune response of T-lymphocytes, acting as the second signal (after antigen) in the immune response. A summary is presented of information on proliferation of normal T-cells in a previously described liquid suspension culture and proliferation of several new cell lines from patients with particular types of T-cell leukemias and lymphomas. Information on the new type-C virus designated HTLV is also summarized. Neoplastic T cells from patients with cutaneous T-cell leukemias and and lymphomas, eg Sezary syndrome and mycosis fungoides, were grown routinely with the use of purified TCGF free of phytohemagglutinin and of lymphokines other than TCGF. The neoplastic T cells responded directly to TCGF without prior in vitro activation with antigen or lectin as is necessary with normal T cells. Thus, transformed mature T cells already express TCGF receptors. HTLV were isolated from some of these new cell lines. Evidence is presented to indicate these may be the first unambiguous isolates of RNA tumor viruses from humans. These new viruses are easily distinguished from all previously isolated viruses from animals. Antibodies in sera of some patients with these diseases specifically react with proteins of these viruses. (11 Refs)

5. CHARACTERIZATION BY NUCLEIC ACID HYBRIDIZATION OF HTLV, A NOVEL RETROVIRUS FROM HUMAN NEOPLASTIC T-LYMPHOCYTES.

Reitz MS, Poiesz BJ, Ruscetti FW, Gallo RC
Natl. Cancer Inst., Bethesda, MD, 20014
Haematol Blood Transfus; 26:515-516 1981

Cyclic DNA (cDNA) and 70S RNA were prepared from the novel human neoplastic T-lymphocyte retrovirus HTLV. These probes were used to determine (1) degree of relatedness to other viruses, (2) whether or not HTLV is endogenous, and (3) whether related sequences can be found in other human tissues. HTLV cDNA hybridized 90% to its own 70S RNA; it did not hybridize significantly to a variety of retroviruses including murine and feline leukemia and sarcoma viruses, baboon endogenous virus, squirrel monkey retrovirus, Mason-Pfizer virus, bovine leukemia virus, RD114 endogenous cat virus, murine mammary tumor virus, and avian myeloblastosis virus. Low (5-10%) levels of hybridization were achieved with 70S from woolly monkey virus and gibbon ape leukemia virus. No HTLV hybridization was obtained with DNA or RNA from normal human peripheral blood T-lymphocytes, with DNA from non- neoplastic autopsy tissues or peripheral blood samples from patients with acute myelogenous leukemia, chronic myelogenous leukemia, or chronic lymphocytic leukemia. DNA from 1/3 acute lymphocytic leukemias (ALL) and 1/2 Sezary syndrome peripheral blood samples hybridized a significant 20-25% of HTLV cDNA. The positive ALL was T-cell. HTLV appears to be a novel retrovirus isolate not endogenous to humans. Results suggest that it is associated with T-cell lymphomas and leukemias of mature cell type. (1 Ref)

6. A VIRUS ASSOCIATED WITH HUMAN ADULT T-CELL LEUKAEMIA.

Weiss R
Inst. Cancer Res., London, England
Nature; 294(5838):212 1981

Recent virological, serological and epidemiological evidence strongly indicates that a newly discovered retrovirus is the etiological agent of certain types of adult T-cell lymphoma/leukemia. The virological evidence first came from RC Gallo's laboratory at the US NCI where the retrovirus was isolated from a T-lymphoma cell line established in culture from a patient with mycosis fungoides. In this issue of Nature Poiesz et al report the isolation of a similar virus from a patient with Sezary syndrome, while Kalyanaraman et al show that the two patients' sera (and that of a patient's spouse) contain antibodies which specifically react with the major core protein of the virus. Mycosis fungoides and Sezary syndrome are clinical variants of cutaneous T-cell lymphoma and leukemia, respectively, that occur as rare diseases in adults. The retrovirus particles produced by these tumors are not evident until the tumor cells are grown in culture, although a second biopsy from the first patient released virus within 24 hr of its being placed in culture. Until 5 yr ago it was very difficult to maintain normal or malignant T cells in culture; however, a specific T-cell growth factor (TCGF) discovered in Gallo's laboratory enables T cells to proliferate in vitro for long periods, and this aided the detection of the virus. (Author abstract) (12 Refs)

7. THE SPECTRUM OF EPSTEIN-BARR VIRUS DISEASE.

O'Dell JR
Dept. Internal Medicine, Univ. Nebraska Medical Center, NE
Nebr Med J; 66(12):275-278 1981

History and pathogenesis of infectious mononucleosis (IM), chronic IM, and other lymphoproliferative syndromes caused by Epstein Barr virus (EBV) are discussed. Primary EBV infection occurs primarily during childhood and is usually asymptomatic. Transmission is through oropharyngeal secretion of EBV by a seropositive individual to a seronegative individual. IM usually persists for 25-30 days, but some individuals suffer from chronic IM possibly due to the presence of early antigen-R antibodies. Primary EBV infection that develops during adolescence can lead to x-linked recessive lymphoproliferative syndrome (Duncan's disease) or possibly Burkitt's lymphoma, Hodgkin's disease, and nasopharyngeal carcinoma. (5 Refs)

EPIDEMIOLOGY AND ETIOLOGY OF HUMAN LYMPHORETICULAR MALIGNANCIES: OTHER STUDIES

8. DOES THE CLASTOGENIC FACTOR IN THE HUMAN GENETIC DISORDER ATAXIA TELANGIECTASIA PLAY A ROLE IN THE DEVELOPMENT OF LEUKEMIA IN HOMOZYGOUS CHILDREN? (MEETING ABSTRACT).

Becker Y, Shaham M
No affiliation given
Tenth International Symposium for Comparative Research on Leukemia and Related Diseases, August 31-September 4, 1981, Los Angeles, California. 187 pp., 1981.

Ataxia telangiectasia (AT) patients have a tendency to develop lymphoproliferative malignancies, and its seems that the heterozygotes in the family have a higher incidence of cancer than the general population. The characteristic of chromosome breakage in cultured skin fibroblasts and lymphocytes from AT homozygotes is used in confirming the diagnosis of AT patients. The presence of the AT clastogenic factor in the amniotic fluid of a pregnant woman who had previously given birth to an AT affected child, has now been demonstrated. Incubation of cell free amniotic fluid from the pregnancy at risk for AT with normal stimulated lymphocytes led to increased chromosome breakage in the test lymphocytes, as compared to control amniotic fluids which caused no increased chromosome damage in normal lymphocytes. The diagnosis that the embryo was homozygous for AT was confirmed by the high chromosome breakage rate of amniotic cells, 15% of which also showed translocations between chromosomes 14 and 5. However, nine wk were required for growing the amniotic cells, before diagnosis was possible, whereas the test for the AT clastogenic factor in the amniotic fluid was done in less than a wk. Apparently, amniotic cells from AT fetuses grow slowly and poorly in culture, as do AT skin fibroblasts. Thus rapid diagnosis of AT in amniocentesis is now possible by testing for the clastogenic factor produced by the embryo. Our hypothesis is that a defective gene in AT patients is responsible for the production of the clastogenic factor. This factor may cause the formation of a clone of cells carrying chromosome translocations which may thereafter become malignant. (no Refs)

9. THE ROLE OF CHROMOSOME ABERRATIONS IN HUMAN CANCER (MEETING ABSTRACT).

Bishun N
No affiliation given, Marie Curie Memorial Foundation, Oxted, England
Teach-In on Research Methods in Cancer, June 30, 1981, London, England Marie Curie Memorial Foundation; 1981

Numerous attempts to elucidate the role of chromosomal changes in carcinogenesis have been made recently and this has been due mainly to the improvement of cytological techniques. The involvement of chromosomes in neoplastic growth, is a natural outcome of Boveri hypothesis which suggested in a more definite form that malignancy was due to an abnormal chromosome content of the cells. The reputed Boveri's Chromosome theory of cancer, suggests that chromosomal aberration is the common pathway through which carcinogenic factors induce cancer. Certain types of cancer, especially the leukemias, are known to occur with a higher frequency in Down's syndrome, in patients with sex chromosome anomalies and in their relatives. The anomalies may predispose these patients directly or indirectly to cancer and, furthermore, is not restricted only to patients with Down's syndrome or sex chromosmoe abnormalities. Certain diseases, considered to be preleukemic conditions, in addition to being carried by a recessive gene, show congenital chromosomal damage and finally develop into leukemia. In another inherited disease, Xeroderma Pigmentosa, the chromosomal aberrations present may be asynchrony of a particular chromosome during the mitotic cycle and could lead to aneuploidy and subsequent malignant transformation. Chromosomal studies and evaluation of mutagenic potential of all new and established drugs, food additives and environmental chemicals should be integral aspects of the current practices of safety evaluation of these substances, and the same str ingent principles should be applied to the numerous chemicals used as solvents and intermediates in industrial processes. Persons exposed to high risk, such as those working in chemical industries, must be monitored constantly using all the methodologies at hand. (no Refs)

10. OTHER IATROGENIC CANCERS (MEETING ABSTRACT).

Ross RK
No affiliation given
The Causes of Cancer, November 6, 1981, Los Angeles, California California Hospital Medical Center; 1981

The majority of iatrogenic cancers fit into two categories: those induced by diagnostic or therapeutic radiation and those induced by prescription drugs. Since radiation induced cancer has already been discussed in detail, this session will be primarily concerned with drugs as causes of human cancer. Several drugs which are now recognized as causes of human cancer have been detected only because of the rarity of the cancer in the absence of the drug. For example, the association between a mother's use of diethylstilbestrol during pregnancy and the development of clear cell adenocarcinomas of the vagina in her daughter decades later was only detected because several cases of this extremely rare tumor were noted in a single hospital in a rather short period of time. Similarly, in a case-control study at University of Southern California, it was demonstrated that risk to women or a rare form of liver cancer, benign liver adenoma, was strongly related to duration of use of oral contraceptives. It seems likely that such relationships exist for more common cancers by go undetected either because no one suspects this relationship or the relationship is difficult to study in the face of other factors causing the same disease. In fact, several such relationships with more common cancer sites have been demonstrated in recent yr. Use of amphetamines has been shown to increase one's risk to Hodgkin's disease some 4-6 fold, use of immunosuppressive drugs has been demonstrated to greatly increase risk to non-Hodkins' lymphomas and use of estrogen replacement therapy, perhaps the most widely studied group of drugs in terms of cancer risk, increases risk of endometrial cancer and breast cancer. (no Refs)

11. INCREASED RISK OF LEUKEMIA IN POLYCYTHEMIA VERA PATIENTS TREATED WITH CHLORAMBUCIL.

Caspary WF, Heimpel H, Von Heyden H
Hanau, W. Germany
Inn Med; 8(5):209-212 1981

Previously published results of a prospective, randomized, controlled clinical study (N Engl J Med 304: 441, 1980) concerning the treatment of patients with polycythemia vera (PV) are summarized by Caspary and discussed by Heimpel and by von Heiden. It is noted that the results indicated that the use of chlorambucil in the treatment of PV increased the rate of development of PV into acute leukemia. Definition, symptoms, and diagnosis of PV are considered, with emphasis on hematologic findings. Conventio nal treatment of PV by surgery or radioactive phosphorus is compared with newer treatments involving the use of myelosuppressive drugs. The danger of acute leukemia development associated with the use of either the radiologic or chemotherapeutic method is discussed. A series of studies designed to identify the optimal treatment for PV are briefly described. Indications and contraindications are listed for the use of the surgical, radiologic, and myelosuppressive treatment of patients with PV. (10 Refs) (In GER)

12. HOW HIGH A PERCENTAGE OF ENVIRONMENTALLY RELATED CANCER CASES CAN BE PREVENTED IN NORWAY?.

Langard S
Yrkesmedisinsk avdeling, Telemark sentralsjukehus, 3900 Porsgrunn, Norway
Tidsskr Nor Laegeforen; 101(28):1602-1606 1981

Approx 110,000 cases of cancer were recorded in Norway during the period 1966-1975. Esophageal cancer was diagnosed in 1.099 cases, gastric cancer in 11,702, cancer of the gastrointestinal tract in 9,270, rectal cancer in 4,670, cancer of the liver and bile ducts in 253, pancreatic cancer in 3,992, larynx cancer in 745, lung cancer in 7,608, prostate cancer in 10,835, renal cancer in 3,191, cancer of the bladder and urinary tract in 4,047, and malignant lymphoma in 3,336. The percentage of environmentally related, ie, preventable cancer was estimated after extrapolation to the 1979 incidence. According to the low estimate, 2,250 cases of cancer were attributable to smoking, 300 to alcohol consumption, and 150 to occupational exposure. (15 Refs) (In NOR)

13. OCCURRENCE OF CANCER IN A SMALL COHORT OF ASBESTOS-EXPOSED WORKERS.

Hilt B, Rosenberg J, Langard S
Dept. Occupational Medicine, Telemark Sentralsjukehus, N-3900 Porsgrunn, Norway
Scand J Work Environ Health; 7(3):185-189 1981

Twenty-one young men of similar age were heavily exposed to asbestos dust during construction of a saltpeter plant from 1928-1929. The asbestos was used to fill grooves between blocks in huge granite towers where nitric acid was to be syn-

thesized and stored. The jointing material was prepared in a room of approx 40 square meters; no ventilation system was used and no equipment for personal protection was available. The dust was so thick that the employees could barely see across the room. Crocidolite asbestos was the type generally used. Av length of exposure was approx 1 yr. In the 21 men, three cases of lung cancer were observed between January 1943 and June 1980; one of stomach cancer, two of malignant mesothelioma, one of myelomatosis, and one of malignant melanoma were also seen. The observed/expected ratio for lung cancer including the pleural mesothelioma was 18.7. The mean latency period for lung cancer was 46 yr; for mesothelioma cases the latency was 22 and 48 yr. All fatal cancers observed in the cohort occurred in smokers (those who smoked during the last 10 yr of their lives); the smoking members of the cohort had a cancer mortality of 43.8% before reaching 65 yr compared with no cancer deaths among nonsmokers. Radiographic changes associated with asbestos exposure were present in 17/18 available chest radiographs. (22 Refs)

14. HYDROCARBONS AND THEIR EFFECTS.

da Silva E
Petroquimica Uniao S/A, Brazil
Saudo Occup Seguranca; 16(1):12-17 1981

The metabolism and toxic effects of aromatic hydrocarbons (AH) are reviewed, tests that monitor exposure are described, and the control of exposure of chemical industry workers to AH is discussed. All AH have acute toxic effects, but only benzene is known to have chronic effects, including reversible leukopenia, severe bone marrow aplasia, and leukemia. The simplest, most efficient tests for monitoring exposure to AH include determining urinary phenol level, which is directly proportional to the concentration of benzene in the workplace, and hemograms. Tolerance limits for exposure to AH of workers in Spain, the United States, and Brazil are compared. Rigorous and periodic medical surveillance of AH-exposed workers in the chemical industry is recommended. (19 Refs) (In POR)

15. MORTALITY AMONG ETHYLENE OXIDE WORKERS.

Morgan RW, Claxton KW, Divine BJ, Kaplan SD, Harris VB
Environmental Health Assoc. Inc., 2150 Shattuck Ave., Suite 414, Berkeley, CA, 94704
JOM; 23(11):767-770 1981

Because of reports linking an increased risk of leukemia with exposure to ethylene oxide, a mortality study of workers with potential exposure to ethylene oxide at the Texaco Chemical Company Plant in Port Neches, Texas, was undertaken. A total of 767 males with potential exposure to ethylene oxide were identified. Forty-six deaths occurred in this cohort with 80 expected [standardized mortality ratio; SMR = 58]. No deaths from leukemia were seen, nor were there any statistically significant excesses from any specific causes of death. (Author abstract) (14 Refs)

16. MORTALITY STUDY OF CHEMICAL PLANTS IN THE KANAWHA VALLEY REGION OF WEST VIRGINIA (MEETING ABSTRACT).

Leet TL
No affiliation given
Second Annual NCI/EPA/NIOSH Collaborative Workshop: Progress on Joint Environmental and Occupational Cancer Studies, September 9-11, 1981, Rockville, Maryland. National Cancer Institute 33 pp., 1981.

The mortality experience of Union Carbide employees at three chemical plants in the Kanawha River Valley region of West Virginia will be evaluated in a study jointly conducted by the National Institute for Occupational Safety and Health (NIOSH) and the Union Carbide Corporation. These plants have produced many chemicals, including acrylonitrile, ethylene oxide, polycyclic aromatic hydrocarbons (PAH), vinyl resins, and pesticides. A company-sponsored proportionate mortality study based on 819 deaths known to Union Carbide found excess proportions of multiple myeloma and cancer of the kidney and CNS. Initial analyses will evaluate the validity of the apparent excesses as well as evaluate all other cause-specific mortality. Further analyses will test the epidemiologic association between 1) ethylene oxide exposure and leukemia and 2) PAH exposure in the coal hydrogenation process and cancer of the respiratory system, urogenital system, and skin. The study cohort includes approx 44,000 employees who were ever employed by Union Carbide in the Kanawha Valley between January 1, 1940 and December 31, 1978. Demographic and work history data have been coded, keypunched, and computerized for 10,000 active and 34,000 former employees. Vital status ascertainment has been initiated and death certificates are being collected for 6,800 (estimated) deceased employees. (no Refs)

EPIDEMIOLOGY AND ETIOLOGY OF NON-HUMAN LEUKEMIA AND LYMPHOMA

17. ROLE OF COLOSTRUM AND MILK IN THE NATURAL TRANSMISSION OF THE BOVINE LEUKEMIA VIRUS.

Ferrer JF, Piper CE
Comparative Leukemia Studies Unit, New Bolton Center, Sch. Veterinary Medicine, Univ. Pennsylvania, Kennett Square, PA, 19348
Cancer Res; 41(12):4906-4909 1981

The role of colostrum and milk in the transmission of the bovine leukemia virus (BLV) was examined by monitoring the development of BLV infection in calves that were fed since birth on colostrum and milk from their BLV-positive dams and then reared in complete or partial isolation from infected cattle. Twenty-one of the 25 calves raised in complete isolation remained negative for BLV until the last evaluation. At this time, 14 calves were older than 28 mo of age, and 7 were 16 to 20 mo old. Three calves in this group became BLV positive before the age of a 5 mo, and one became so at the age of 12 mo. Of the 16 calves raised in partial isolation, 2 were positive at the ages of 11 and 18 mo, respectively. The other 14 calves remained negative during the 26 to 29 mo of observation. It is not known if the six animals that became BLV positive in these two groups were infected by milk, or prenatally, or during contact with their infected dams. While only 6 of the 41 calves raised in isolation became infected, all 18 calves raised in contract with BLV-positive cows became infected before the age of 26 to 29 mo of age, and 12 were positive at 16 to 20 mo of age. Thus, it is apparent that, under natural conditions, milk-borne transmission of BLV, if it occurs at all, is much less frequent than contact transmission, despite the fact that, as shown in previous studies, infectious BLV is present in the colostrum and milk of most BLV-positive cows. Passively acquired maternal antibodies to BLV were probably responsible for the resistance of the calves to milk-borne infection. (Author abstract) (21 Refs)

18. STUDIES ON THE ASSOCIATION OF A FILTERABLE AGENT WITH BUFFALO LYMPHOSARCOMA (MEE TING ABSTRACT).

Singh CM, Bansal MP, Singh KP
No affiliation given
Tenth International Symposium for Comparative Research on Leukemia and Related Diseases, August 31-September 4, 1981, Los Angeles, California. 187 pp., 1981.

Studies on Bovine lymphosarcoma/leukemia particularly in Indian buffaloes have been carried out for the last several yr at this Institute. Clinico-pathological aspect involving various organs have been recorded in detail and published elsewhere. It has been observed that a filterable agent which replicates in buffalo lymphocyte cell culture is associated with this syndrome. However, this agent is not similar to viruses of enzootic bovine leukemia, gibbon ape leukemia and murine leukemia as observed by immuno-diffusion, radio-immunoprecipitation and radio-immune assay which indicate that agent associated with buffalo might have a different antigenic configuration. In the present communication the observation on etiopathological aspects of this syndrome in buffalo are presented and discussed. (4 Refs)

19. ROLE OF VIRUSES IN THE ETIOLOGY OF NATURALLY OCCURRING FELINE LEUKEMIA.

Essex M, Grant CK, Cotter SM, Hardy Jr WD
Dept. Microbiology, Harvard Sch. Public Health, 665 Huntington Ave., Boston, MA, 02115
Haematol Blood Transfus; 26:483-487 1981

The biology and natural history of the feline retroviruses and the diseases they cause are reviewed. The feline leukemia viruses (FeLV) cause several forms of leukemia and lymphoma that occur at different rates in different geographic areas; no specific association between naturally occurring disease and any strain(s) of any subgroup(s) has been demonstrated. FeLVs are replication competent and cause no visible pathology in infected cultured cells. FeLVs are transmitted in a contagious manner. Approx 2-5% of infected cats become persistently viremic, and one-fourth to one-third of these animals develop leukemia (the other develop infectious peritonitis, septicemia, or glomerulonephritis). Both leukemic and persistently viremic cats release large amounts of infectious FeLV in their saliva. FeLV appears to play an important role in the etiology of 'virus-negative' leukemia in cats; an understanding of the mechanism of this phenomenon may help us to explain human leukemias that occur in individuals that do not harbor replicating virus. FeLV particles contain seven distinct proteins, several of which have greater than 1 antigenic determinant and all of which induce immune responses in cats to some degree. The feline oncornavirus-associated cell membrane antigen (FOCMA) is found on lymphoma and/or leukemia cells, and the immune response to it is correlated with protection against development of leukemia and lymphoma. Two general classes of tumor- and transformation-specific antigens have been found. (39 Refs)

20. PREVALENCE AND SEQUELAE OF FELINE LEUKEMIA VIRUS INFECTION IN LABORATORY CATS.

Ladiges WC, DiGiacomo RF, Wardrop KJ, Hardy WD
Div. Animal Medicine, Univ. Washington, Seattle, WA, 98195
J Am Vet Med Assoc; 179(11):1206-1207 1981

Over a 4-yr period, 1,683 pound-source cats received at a research institution were screened for feline leukemia virus (FeLV) infection, using an indirect fluorescent antibody test. Viremia was detected in 83 of the cats, for a prevalence of 4.9%. During this period, FeLV infection was detected in five kittens on a research project; lymphoma or anemia developed 6 to 17 mo after the infections were detected. It was concluded that apparently healthy cats infected with FeLV may not be appropriate for some biomedical research projects. (Author abstract) (9 Refs)

21. QUANTITATIVE CHANGES IN AKR THYMOCYTE SUBSETS PRECEDING THE ONSET OF LEUKEMIA.

Fournier M, Potworowski EF, Kowalczyk D
Immunology Res. Center, Institut Armand-Frappier, Post Office Box 100, Laval, Quebec H7N 4Z3, Canada
Immunobiology; 159(4/5):382-390 1981

The evolution of T-cell subsets in the thymuses of leukemia-prone AKR and of non-leukemia-prone BALB/c mice was compared for a period of 9 mo. In AKR mice there is a sharp rise in thymic hormone sensitive thymocytes bearing a high concentration of Thy 1 antigen. While these cells also rise with age in BALB/c mice, they do so more slowly. The response of thymocytes to Con A was also compared between the two strains: the response of AKR cells drops to below significant levels within 7 mo, while BALB/c cells remain reactive throughout the experimental period. Since these age-related changes in Thy 1 antigen density and Con A reactivity can be reversed after incubation with a thymic hormone preparation, it is concluded that they are the result of a decrease in thymic hormone secretion, that this decrease is much more pronounced in AKR mice than in BALB/c mice and may therefore play a role in the etiology of the AKR leukemia. (Author abstract) (32 Refs)

22. INDUCTION OF LYMPHOMA IN ANTIGENICALLY STIMULATED ATHYMIC MICE.

Baird SM, Beattie GM, Lannom RA, Lipsick JS, Jensen FC, Kaplan NO
Dept. Pathology, Veterans Admin. Medical Center, San Diego, CA, 92161
Cancer Res; 42(1):198-206 1982

Athymic mice infected with pinworms or carrying human tumor xenografts frequently develop a lymphoproliferative disorder which eventually leads to lymphoma. By immunofluorescent analysis of involved tissues, the lymphomas appear to be mixtures of null cells, B-cells, and T-cells. When each lymphoma is established in tissue culture, a predominant cell type grows out. We have now established lymphoma lines of null cells, B-cells, and T-cells. Lymphoma development is preceded by the secretion into the bloodstream of large amounts of murine leukemia virus mol wt 70,000 glycoprotein antigen; however, very little virus is produced. In vivo, the expression of viral envelope antigen appears within a few days after human tumor transplantation and precedes the development of lymphoma by about a mo. Cells expressing viral antigens are first seen in the diffuse cortex of lymph nodes and the periarteriolar white sheath of the spleen, the tissue domains in which lymphomas also first appear. (Author abstract) (21 Refs)

23. CHROMOSOME REARRANGEMENTS INVOLVED IN THE ORIGIN OF TRISOMY 15 IN SPONTANEOUS LEUKEMIA OF AKR MICE.

Herbst EW, Gropp A, Tietgen C
Institut fur Pathologie, Medizinischen Hochschule Lubeck, Ratzeburger Allee 160, D-2400 Lubeck, W. Germany
Int J Cancer; 28(6):805-810 1981

Trisomy 15, known to be the predominant chromosome abnormality in leukemic cells of the AKR strain, develops even in animals of the subline AKR/RblAld with two constitutive Robertsonian translocation chromosomes (6.15). Among 10 leukemic animals of this subline exhibiting chromosomal anomalies, 6 showed trisomy of the whole Robertsonian translocation chromosome with the expression of combined trisomy 6 and 15 as the most frequent abnormality. Besides this, rearrangements were observed in five animals, most of them resulting from centric fission of the RB(6.15) translocation chromosome. Trisomy 15 with two Rb(6.15) and an extra acrocentric 15 was found in 44% of spleen cells in one animal, and a new Rb translocation of chromosomes 11 and 15 were seen in 50% of spleen and thymus cells of another animal. In both cases trisomy 15 without simultaneous trisomy 6 resulted. Thus, the triplication of a whole Rb(6.15) is frequent in leukemic AKR/Rb(6.15)lAld, and ensuing double trisomy 6 + 15 is tolerated by the leukemic cell. But the development of trisomy 15 combined with centric fission of Rb(6.15) without simultaneous trisomy 6 is another principle realized in leukemogenesis. (Author abstract) (19 Refs)

24. CHARACTERIZATION OF A RETROVIRUS-LIKE AGENT ISOLATED FROM A CASE OF CANINE LYMPHOMA (MEETING ABSTRACT).

Strandstrom HV, Graef P, Bowen JM
No affiliation given
Tenth International Symposium for Comparative Research on Leukemia and Related Diseases, August 31-September 4, 1981, Los Angeles, California. The Association 187 pp., 1981.

This report describes results of studies designed to isolate and identify virus like agents from a canine lympho-proliferative diseases. A continuous cell line was established from the ascites fluid of a dog with malignant lymphoma. The cells grow in suspension, produce immunoglobulins, exhibit phagocytic activity, and agglutinate in the presence of phytohemagglutinin and concanavalin A. The dog lymphoma cells (3132) in culture incorporate 3H-uridine into particles banding at a density of 1.16-1.17 g/cm3 in sucrose. These particles contain a high mol wt 60-70S RNA. RNA dependent DNA polymerase (RT) activity was detected in detergent disrupted particles released by the cell line. The activity was found to be present in the density range of 1.16-1.17 g/cm3. The RT had a cation preference characteristic of type C viruses. The putative retrovirus particles had a major protein component which on sodium dodecyl sulfate-polyacrylamide electrophoresis had a mol wt of about 30,000 daltons. The 30,000 dalton protein focused at pH 7.6. When the particles were surface-labeled by the lactoperoxidase technique, and the radiolabeled particles run on gels, the major radiolabeled peak correspond to a mol wt of 70,000 daltons. Biological activity of the canine particles was studied both in vitro and in vivo. The only cell lines found to be susceptible to infection by the canine agent were of canine and normal human origin. The virus could not be demonstrated in the target cells before inoculation, but grew to high titers and appeared to be stable incorporated in the cells, although no morphological transformation could be demonstrated. The canine agent was also inoculated into newborne puppies. Although no pathological changes could be observed in the inoculated puppies at autopsy, cell lines were initiated from organs from these puppies. Successful cultures were obtained only from dogs inoculated with the 3132 agent. The cultures from these dogs (2 dogs) consisted of one derived from spleen and one derived from bone marrow. Both cell lines produced viral particles with biochemical and antigenic characteristics of the original 3132 particles. The data suggest that the canine particles are retroviruses related to but distinguishable from simian retroviruses. (no Refs)

CYTOGENETIC AND MORPHOLOGIC STUDIES

25. CLONAL ORIGIN OF LEUKEMIA: SITE OF ORIGIN IN THE STEM CELL HIERARCHY AND THE SIGNIFICANCE OF CHROMOSOMAL CHANGES.

Boggs DR, Lajtha L, Brecher G, Bernard J, Gallo R, Bessis M, Greaves MJ, Van Beddum DW, McCulloch EA
Dept. Medicine, Univ. Pittsburgh, Sch. Medicine, Pittsburgh, PA, 15261
Blood Cells; 7(2):205-215 1981

The strongest evidence that hematologic neoplasms are clonal is derived from analysis of cells in patients heterozygous for A and B isozymes of glucose-6-phosphate dehydrogenase. Clonality of chronic lymphoid leukemia is also suggested by studies of surface immunoglobulin of cells of most patients. Clinical and other data are presented as to possible site of origin of cancer in the hematopoietic stem cell hierarchy. Data are presented which suggest that chromosome abnormalities and morphologic abnormalities are not necessarily present uniformly throughout the clone. Thus, normal appearing, chromosomally normal cells may be part of the clone in acute and chronic myeloid leukemia; in some patients both abnormalities may exist as independent variables. If it should be proven the chromosome abnormality is only a subpopulation of the leukemic clone, then that abnormality cannot be considered the cause of leukemia. However, the abnormality could still represent an epiphenomenon of genetic damage in that chromosome or another chromosome, which was responsible for leukemic development and which also was expressed by visible chromosomal abnormalities in certain cells. (10 Refs)

26. DOWN SYNDROME AND ACUTE LEUKAEMIA: INCREASED RISK MAY BE DUE TO TRISOMY 21.

Rowley JD
Section Hematology/Oncology, Dept. Medicine, Univ. Chicago, Chicago, IL, 60637
Lancet; 2(8254):1020-1022 1981

Individuals with Down syndrome (DS), especially children, have an increased incidence of acute leukemia. It is suggested that this increased risk is specifically associated with the presence of an extra chromosome 21 (+21) as a constitutional abnormality. Data available from surveys of non-DS patients with acute lymphocytic leukemia (ALL) and acute non-lymphocytic leukemia (ANLL) indicate that a +21 is the most common change in leukemic cells in ALL, especially in children, and that it is one of the more common changes in ANLL. In neonatal patients with mosaicism for normal cells and +21 cells who have a transient leukemoid reaction, the blast cells involve the +21 clone; spontaneous disappearance of the leukemoid reaction parallels a decrease in +21 cells in

the bone marrow. Thus, the increased risk of acute leukemia in patients with DS who have a +21 is directly related to the presence, in all cells of these individuals, of the same chromosome change that is commonly seen in the leukemic cells of children with ALL, the type of leukemia most commonly seen in DS children. This observation is analogous to that for two other constitutional chromosome abnormalities that are associated with an increased risk of a malignant tumor. A deletion of chromosome 13, including band 13q14 is associated with retinoblastoma, and a deletion of chromosome 11, including band 11p13 is associated with aniridia/Wilms tumor syndrome. The nature of the genes affected by these various chromosome aberrations is unknown. (Author abstract) (20 Refs)

27. PHILADELPHIA CHROMOSOME POSITIVE BLOOD B LYMPHOCYTES IN CHRONIC MYELOCYTIC LEUKEMIA.

Bernheim A, Berger R, Preud'homme JL, Labaume S, Bussel A, Barot-Ciorbaru R
(c/o Berger) Laboratoire de Cytogenetique, Centre Hayem, Hopital Saint-Louis, 75475 Paris Cedex 10, France
Leuk Res; 5(4/5):331-339 1981

An assay was developed to determine by combined study, using surface immunofluorescence and Q banding, the presence of surface immunoglobulins (SIg) on Philadelphia chromosome (PH1)+ mitotic cells obtained by stimulation of blood mononuclear cells by B cell mitogens. Cells were obtained f rom 18 patients (11 men, 7 women, 26-76 yr old) with typical PH1+ chronic myelocytic leukemia. Clear-cut results were obtained in eight cases. The incidence of Ph1+ and Ph1-mitoses was similar in the combined assay and in the regular cytogenetic study. No problems were encountered with SIg staining; the numbers of SIgM-bearing cells were the same in the combined assay in the controls with direct surface staining alone. In the combined assay, Ph1+ SIgM+ cells were found in all patients but only in stimulated cultures. Their presence was associated with B cell stimulation. With the exception of one culture, all SIgM-bearing cells with identifiable chromosome morphology had the Ph1 marker. In unstimulated cultures, every mitosis contained the Ph1 as shown by both single and combined chromosomal analyses. The combined study showed that these spontaneously dividing leukemic cells lacked SIgM. In contrast to control experiments, cultures stimulated with pokeweed mitogen or L881 fraction from Nocardia opaca contained a large number of Ph1-SigM- mitotic cells which were probably stimulated T-cells. (17 Refs)

28. DOUBLE MINUTE CHROMOSOMES IN HUMAN LEUKEMIA.

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Diss Abstr Int [B]; 42(4):1310-B 1981

Cytogenetic studies were performed in 376 patients. Forty patients (11%) were found to have double minute (DM) chromosomes either in direct bone marrow or unstimulated blood WBC preparations. Patients with DM generally could be classified into four diagnostic categories: preleukemia and and myeloproliferative disorders, acute leukemia, chronic or blastic phase myelogenous leukemia and previous malignancy with a leukemic complications. Fourteen of the 40 cases had received treatment with either single agent or combined modality therapy prior to cytogenetic examination. The highest incidence of DM was found in the group of patients who presented with leukemic complication following treatment for a previous malignancy. Chromosome abnormalities were found in 63% of patients in this group; of these cases, nearly 60% had DM. In patients with potentially leukemic disorders (preleukemia) and myeloproliferative diseases, one-third of the patients studied had chromosome abnormalities, and of this group, 30% were found to have DM. In patients with acute leukemia, 63% showed cytogenetic abnormalities; of these patients, 20% had DM. The incidence of DM was found to be lowest in patients with chronic myelogenous leukemia (CML). In 60 cases with Philadelphia chromosome positive CML, 10% were found to have DM in addition to the Ph1 + abnormality. (no Refs)

29. THE 5Q- CHROMOSOME IN PRELEUKAEMIA AND ACUTE LEUKAEMIA.

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Scand J Haematol; 27(2):119-129 1981

Thirteen patients with the 5q- chromosome are described. In six patients the 5q- chromosome was the sole aberration. Ten patients had preleukemia, 1 a preleukemia-like syndrome after treatment of polycythemia vera, a 2 acute myeloid leukemia. The prognosis was especially poor in terms of survival in preleukemic patients with three or more affected chromosomes: none of these six patients survived for more than 6 mo. In four patients the hematological picture resembled 'the 5q- syndrome'. In the long arm of chromosome No. 5 deletions of three different kinds were detected. They were named according to the size of the 5q- marker: the short type (10 patients), the intermediate type (1 patient) and the long type (2 patients). There was no clear correlation between the clinical picture and the type of deletion. While the break points cannot always be exactly defined, our data and those reviewed from the literature suggest that the loss of a segment of regions 5q2 or 5q3 is common to all or most deletions. (Author abstract) (33 Refs)

30. POSSIBLE MULTICLONAL ORIGIN IN THE EARLY STEPS OF THE PRELEUKEMIC PROCESS.

Benitez J, Sanchez Fayos J, Tome P, Ayuso C, Jimenez A
Servicio de Genetica, Fundacion Jimenez Diaz, Av. Reyes Catolicos, 2. Madrid-3, Spain
Sangre (Barc); 26(5A):556-566 1981

The cytogenetic results of four preleukemic stages, which have been studied in several controls, are presented. Some altered cell lines in two of these cases were observed, suggesting a multiple mutation involving several cell clones in early periods of the process, and another posterior selection in one of them, which could favor the development and establishment of the neoplasia. (Author abstract) (17 Refs) (In SPA)

31. KARYOTYPES AND CELL PHENOTYPES IN ACUTE LEUKEMIA FOLLOWING OTHER DISEASES.

Berger R, Bernheim A, Daniel MT, Valensi F, Flandrin G, Brecher G, Van Bekkum DW, Bernard J, Breton-Gorius J, Dreyfus B, McCulloch EA
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Blood Cells; 7(2):293-299 1981

Analysis for cytological and cytogenetic characteristics of acute lymphoblastic leukemias following other blood diseases or exposure to carcinogens revealed that some secondary acute leukemias were unclassifiable in the FAB (French, American, British) system. Monosomy 7 was associated with megakaryocyte abnormalities. These cytological and cytogenetic vari-

ations were studied in pooled samples from patients with acute nonlymphocytic leukemia and in similar patients following polycythemia vera. (8 Refs)

32. KARYOTYPE AND CELL PHENOTYPES IN PRIMARY ACUTE LEUKEMIAS.

Berger R, Bernheim A, Daniel MT, Valensi F, Flandrin G
Laboratoire de Cytogenetique, Centre Hayem, Hopital Saint-Louis, 75475 Paris Ced ex 10, France
Blood Cells; 7(2):287-292 1981

Chromosomal and cytological patterns in acute leukemias (AL) and attempts to correlate them with the FAB (French, American, British) classification are reviewed. Despite the realization that the FAB classification is an oversimplification, the studies are useful in distinguishing different forms of AL and understanding the nature of the cell type from which the malignant clone originated. Thus, studies of acute promyelocytic leukemia provide a likely explanation for lack of chromosome abnormalities in certain cases of AL. (13 Refs)

33. CYTOGENETICS IN THE ACUTE LEUKEMIAS.

Prieto F, Badia L, Castell V, Perez-Sirvent ML, Marty ML
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Sangre (Barc); 26(5B):738-755 1981

Out of 64 cases of acute leukemia (47 non-lymphoblastic and 17 lymphoblastic ones) in which cytogenetic studies were performed, 30 had normal karyotype (22 non-lymphoblastic and 8 lymphoblastic). The acute non-lymphoblastic leukemias with normal karyotype had a mean survival close to 11 mo, as opposed to 2-1/2 mo for the cases in which all the leukemia cells had abnormal karyotypes. The nine patients with WBC count above 100,000/cu mm had survivals slightly over 4 mo in spite of the normal karyotype found in seven of them. Chromosome 8 trisomy was the commonest numeric alteration, and it was seen n both leukemia groups; t(8q-; 21q+) associated to loss of the Y chromosome was found in a patient with M2 non-lymphoblastic leukemia, and this represents a 2% frequency in the series. Two patients with L3 lymphoblastic leukemia showed the same structural alteration, t(8q-; 14q+); one of them had other cytogenetic anomalies including two acrocentric marker chromosomes comprised of genetic material from chromosome (1(q21 q44)) translocated into a Y gonosome. The similarity of both cases with those of Burkitt lymphoma from a clinical, cytological, and cytogenetic standpoint is further evidence in support of the identity of L3 lymphoblastic leukemia and Burkitt lymphoma, which could be regarded as different manifestations of a unique disease status. (Author abstract) (58 Refs) (In SPA)

34. CHROMOSOMAL ABERRATIONS IN LYMPHOPROLIFERATIVE DISEASES.

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Medicina (B Aires); 41(3):297-300 1981

The 25 patients studied were diagnosed as: 8 non specific lymphadenitis, 2 giant follicular hyperplasia, 5 Hodgkin's disease, and 10 non-Hodgkin's lymphoma. The lymphadenitis patients (5 women and 3 men) had normal karyotypes: 40, XX and 46, XY respectively, they were the control group. The two cases of giant follicular hyperplasia had non specific number anomalies affecting different chromosomal groups. The five Hodgkin's disease patients, all had number anomalies, two were specific clones: one with 15q+ marker and one with complete 21 trisomy. Of the 10 non-Hodgkin's lymphomas: 7 were little differentiated diffuse lymphocyte lymphomas, and 3 well differentiated nodular lymphocyte lymphomas, all with important chromosomal anomalies. Half of them had numerical or structural anomalies of chromosome 1, which caused partial or total trisomies in the long part of that chromosome, recurrent markers were 1q+, 1p+, ans 1+. Of the other patients two had 14q+ marker, one had 6q- marker, two were clones with one and two chromosomes respectively in a ring. (16 Refs) (In SPA)

35. IMPORTANCE OF CYTOGENETIC ALTERATIONS IN NEOPLASTIC TRANSFORMATION IN LYMPHOMAS.

Slavutsky IR
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Medicina (B Aires); 41(3):382-385 1981

This general overview of lymphomas' cytogenetic studies stresses importance and specificity of 14q+ marker with its 50% frequency in lymphomas (L), t(8q-;14q+) characteristic of Burkitt lymphoma and t(11q-; 14q+) of lymphosarcoma. L could be characterized according to 14q+ translocations or to different markers detected. Correlation between cytogenetic examination and clinical staging should be established. Cytogenetic studies should contribute to the clarification of histological classification and therapy response. (no Refs) (In SPA)

36. SISTER-CHROMATID EXCHANGES BEFORE AND AFTER HAIR DYEING.

Kirkland DJ, Honeycombe JR, Lawler SD, Venitt S, Crofton-Sleigh C
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Mutat Res; 90(3):279-286 1981

Cytogenetic changes were evaluated in peripheral lymphocytes of 14 volunteers (13 women and 1 man) after a single application of hair dye. Six hr after dyeing, six volunteers showed increases and eight showed decreases in mean number of sister-chromatid exchanges (SCE). No statistically significant differences were observed in mean SCE/cell between predyeing samples and those taken at 6 hr or 7 days after dyeing. (15 Refs)

37. THE APPLICABILITY OF SIMPLE BLOOD AND BONE MARROW VARIABLES IN PREDICTION OF ACUTE LEUKAEMIA IN PATIENTS WITH ACQUIRED BI- OR PANCYTOPENIA.

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Scand J Haematol; 27(3):193-200 1981

A retrospective study of 44 patients presenting with acquired bi- or pancytopenia (B/PC) and no evidence of any causal disorder was carried out. Twelve patients developed acute nonlymphoblastic leukemia after 2-51 mo. Compared to the nonleukemic subjects the preleukemic patients at the onset of B/PC had significantly higher counts of myeloblasts and other myelopoietic cells in the bone marrow, more cellular marrows due to more dense cellularities of all compartments, higher blood granulocyte and monocyte counts, more pronounced anisocytosis, and in some cases a small number of circulating myeloblasts. A stepwise multiple logistic regression analysis identified three combinations of variable displaying significant simultaneous association with subsequent leukemic transformation. Among these the combination of marrow myeloblast per-

centage and blood granulocyte count might be applicable to early prospective identification of patients with preleukemic B/PC. (Author abstract) (18 Refs)

38. SIDEROBLASTIC ANEMIA AND DEVELOPMENT OF LEUKEMIA.

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Blut; 42(4):203-207 1981

Sideroblastic anemia (SBA) and its relationship to leukemia are reviewed. Sideroblasts (SB) consist of two types of normoblasts with abnormal accumulations of iron. Intermediate, or ferritin, SB contain greater than 6 iron grains and may account for up to 14% of normal bone marrow erythroblasts. Ring SB contain large iron granules forming a perinuclear ring and do not occur in normal bone marrow. Intermediate SB are a nonspecific sign of erythropoietic disorder. Accumulations are found in dyserythropoietic states, including megaloblastic anemia, thalassemia, and refractory anemias involving impaired iron utilization. Ring SB occur in four types of refractory anemia: (1) hereditary, (2) primary acquired, (3) toxic secondary, and (4) premalignant or malignant. The first three types are marked by benign clinical course, dimorphic RBC population, erythroid hyperplasia in the marrow, reduced RBC production, normal colony formation in vitro, and normal or high platelet count. Preleukemic SBA is usually accompanied by disturbances of other blood cell lines. SB count and classification and recognition of exposure to mutagenic or toxic agents are important in the diagnosis of refractory anemias. (38 Refs)

39. THE ROLE OF GENE DOSAGE AND GENETIC TRANSPOSITIONS IN CARCINOGENESIS.

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Nature; 293(5839):313-318 1981

Analysis of chromosome translocations associated with B-cell derived tumors and studies of chromosome-15 trisomy in murine leukemia support the theory, emerging from recent work on tumor viruses, that cancer can be associated with DNA rearrangements which result in the increased expression of normal cellular genes. (Author abstract) (87 Refs)

BIOCHEMICAL, IMMUNOLOGICAL AND OTHER CELL BIOLOGY STUDIES

40. DEVELOPMENTAL HIERARCHY OF IMMUNOGLOBULIN GENE REARRANGEMENTS IN HUMAN LEUKEMIC PRE-B-CELLS.

Korsmeyer SJ, Hieter PA, Ravetch JV, Poplack DG, Waldmann TA, Leder P
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Proc Natl Acad Sci USA; 78(11,part2):7096-7100 1981

We have used a special class of human acute lymphocytic leukemias, the common 'non-T/non-B' cell type, to define a hierarchy of genetic rearrangements that occur during the earliest stages of B-cell maturation. This has allowed us to identify intermediate cells predicted by a hierarchial model in which Ig heavy chain variable region gene formation precedes that of light chain and in which kappa light chain gene formation precedes that of lambda. The model emphasizes the flexible nature of Ig gene recombination that not infrequently produces aberrant or null genes that are phenotypically excluded from expression. Remaining alleles or isotypic genes can then be utilized as 'spares' undergoing recombination until a valid gene is formed. Significantly, the excluded allele or isotype is frequently deleted from the genome. In addition to defining a pathway of genetic maturation, this analysis provides a powerful means to further classify cases of non-T/non-B-cell acute lymphocytic leukemia, most of which seem to reside at early stages along the B-cell pathway of differentiation. (Author abstract) (44 Refs)

41. DEPRESSED IMMUNITY AND THE DEVELOPMENT OF CANCER.

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Clin Exp Immunol; 46(3):459-474 1981

Epidemiological, clinical, and experimental studies of depressed immunity and cancer are reviewed. Topics include transplantation of tumors, cancer in patients with naturally occurring immunodeficiency disorders, de novo cancer in organ transplant recipients, and cancer in uremic patients. Patients with autoimmune and other diseases treated with immunosuppressive agents have increased cancer incidence. Second cancers, particularly leukemias, are more frequent in patients treated with chemo- and radiotherapy. Disturbances in immunity as causes of cancer are presented; immune surveillance, immune stimulation, chronic antigenic stimulation, defective immunoregulation, spontaneous regression of lymphomas, interferons, oncogenic viruses, oncogenic and co-oncogenic effects of immunosuppressive and cancer therapeutic agents, and other potentially oncogenic treatments (UV and arsenic for psoriasis) are discussed. Animals and patients vary in their susceptibility to oncogenic stimuli. Evidence suggests that the immune system plays a key role in host defense against cancer, but many unanswered questions remain. (149 Refs)

42. IMMUNODEFICIENCIES IN HODGKIN'S DISEASE. PART I: T CELL-MEDIATED IMMUNITY.

Gupta S
Clinical Immunology Service, Sloan-Kettering Inst., New York, NY
Clin Bull; 11(2):58-65 1981

The association between Hodgkin's disease and immunodeficiency states is reviewe d. Immunodeficiencies may predispose patients with Hodgkin's disease to a second neoplasm and to increased risk of infectious complications, especially viral and fungal (eg herpes zoster and cryptococcosis). Both in vivo and in vitro T cell-mediated immune responses in patients with various stages of Hodgkin's disease are discussed, including delayed type hypersensitivity, homograft rejection, lymphocyte response to soluble antigens and to mitogens and allo-antigens, analysis of T cells and T cell subsets, and cytotoxic response and mechanisms responsible for T cell-mediated immunodeficiencies. The role played by splenectomy in treatment of Hodgkin's disease is discussed. (71 Refs)

EXPERIMENTAL STUDIES INVOLVING CHEMICAL AGENTS AND IRRADIATION

43. EARLY CHANGES OF HEMATOPOIETIC TISSUES IN MICE TREATED WITH INTRAVENOUS PULSE-DOSES OF 7,12-DIMETHYLBENZ(A)ANTHRACENE.

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Acta Pathol Jpn; 31(5):799-814 1981

Repeated intravenous injections of 7,12-dimethylbenz(a)anthracene (DMBA), 4x weekly, induced several kinds of tumors in 26 mice (83.9%) out of 31 ddO mice, including 13 leukemias and 6 ovarian tumors. All leukemias were of lymphatic type, and 9 cases out of 13 leukemias were of thymus type. The thymus was involved by leukemic cells in 12 cases. All ovarian tumors were diagnosed as granulosa cell tumors histologically. During the treatment of DMBA, two types of changes in organs and blood were observed: one was a striking decrease of wt of organs or number of cells followed by prompt recovery as found in the spleen, red blood cells, and granulocytes in the peripheral blood; the other was moderate but long-standing decrease with little recovery as found in the thymus, ovaries, uterus, and lymphocytes in the peripheral blood. Unlike DMBA, the wt of the thymus was strikingly decreased by prednisolone, one of corticosteroids, whereas reactions of the spleen and the lymph nodes were not remarkable. Autoradiographical studies revealed a severe reduction followed by a marked rebound of labeling index in the red pulp of the spleen, but not in the white pulps of the spleen and cortex of the thymus. From these observations, it is concluded that a mild but long standing injury was noticed in the tissues which were the main sites of the tumorigenesis in mice by DMBA, and a severe but transient injury may not be related to induction of tumors in mice by DMBA. (Author abstract) (14 Refs)

44. CYTOGENETIC CORRELATES OF LEUKEMOGENESIS IN RATS: SHORT- AND LONG-TERM EFFECTS OF 7,12-DIMETHYLBENZ(A)ANTHRACENE ON CHROMOSOME BANDING.

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Diss Abstr Int [B]; 42(4):1313-B 1981

The hypothesis tested in this dissertation is that a correlation exists between the vulnerable chromosome sites of acute damage induced in marrow cell chromosomes by the carcinogen 7,12-dimethylbenz(a)anthracene (DMBA) and the pattern of altered chromosomes found in the marrow cells of rats made leukemic by DMBA. Chromosome banding techniques which permit identification of the individual rat chromosomes were instituted for this study. The location of chromosome alterations can be specified with regard to bands, sub-bands and banding regions. In short-term (acute) experiments, DMBA induced in high incidence of chromosome breaks. On banded chromosomes, breaks were distinguished from light bands only when chromosomes were stained sufficiently dark or when banding on sister chromatids was not aligned. Some chromatid breaks appeared to be intercalary deletions; other breaks appear to be without deletion (loss of substance) but with the chromosome axis malaligned. Breaks in the terminal regions were common. The chromatid breaks induced by DMBA were shown to be nonrandom and were highest in chromosome regions 2q2, 6q2, 1p1, 1q3, 5q3, 4q2, 6q1, and 12p1. These data indicated that the damage induced by DMBA is nonrandom, some chromosome regions showed greater vulnerability to damage by DMBA. Markers chromosomes in leukemic marrow cells involved t(1;2); t(1;4); t(1;6); t(1;7); t(1;9), with each associated with one normal chromosome 1 (monosomy 1p) and two normal number 2, No 4, No 6, No 7, or No 9 chromosomes. Trisomy No 2, 16 and 20 and monosomy No 5, 6, 10 and 18 occurred in leukemic rats but not in control rats. The data presented suggest that leukemogenesis by DMBA requires specific changes at multiple (ie, combination) chromosome sites. The number of these postulated critical sites required in the combination is not known, but our data identify the following morphologic regions as likely to contain these sites: 1q2, q3; the pericentromeric region of No 2 chromosome; 4q4; 5q3; 6q1; 6q2; 9q3; 11p; 12p; and 12q1. (no Refs)

45. INCIDENCE AND TYPE OF TUMORS INDUCED IN C57BL BG/BG MICE AND +/BG LITTERMATES BY ORAL ADMINISTRATION OF DMBA.

Argov S, Cochran AJ, Karre K, Klein GO, Klein G
Dept. Tumor Biology, Karolinska Institutet, S 104 01 Stockholm, Sweden
Int J Cancer; 28(6):739-746 1981

As an attempt to study the effect of the beige (bg) mutation on chemical carcinogenesis, 64 C57Bl/bg/bg mice and 83 +/bg littermate controls received DMBA in five weekly intragastric doses. The incidence of tumors of different histological types was monitored through observation periods ranging between 165 and 500 days. By 165 days after the first DMBA feeding, 18% of the +/bg and 31% of the bg/bg mice had developed tumors. The beige mice had a higher incidence of epithelial and non-epithelial tumors arising in cutaneous or sc sites than the controls. The total incidence of lymphomas was similar in the two group s. However, lymphomas appeared somewhat earlier in beige than in control mice. Altogether 33 +/bg and 27 bg/bg mice were followed for 500 days. By this time, 73% of the +/bg and 78% of the bg/bg mice had developed tumors. The beige group showed a higher incidence of non-thymic lymphomas than the controls. In contrast, the incidence of thymic lymphoma, cutaneous epithelial tumors and bile-duct adenomas was similar in the two groups or higher in +/bg than in bg/bg mice. The results suggest that the bg mutation causes a certain defect in a mechanism that may prevent or delay the onset of nonthymic lymphomas and of epithelial and non-epithelial cutaneous tumors in DMBA-treated mice. The differences between the two groups were smaller than those previously reported in relation to the increased susceptibility of beige mice to certain transplanted tumors, attributed to the known defect in natural killer (NK) activity in the beige mice. The reduced differential in the DMBA system may be due to the partial reduction of NK activity, induced by the carcinogen, as reported previously and confirmed in the present study. (Author abstract) (33 Refs)

46. LEUKEMOGENIC EFFECT OF URETHANE ADMINISTERED TOGETHER WITH ESTROGENS TO MICE.

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Egeszsegtudomany; 25(3):251-255 1981

Effects of carcinogenic and noncarcinogenic substances administered together with estrogens or urethane were studied in

6-8-wk-old male CFLP mice. Each substance was administered in three individual doses during an 18-day period, and the results were evaluated after 300 days. Lung tumors and lymphomas were found in the animals treated with ethyl formate (500 mg/kg), phenylurethane (100 mg/kg), pyrene (5 mg/kg), and their combinations with diethylstilbestrol (DES: 25 mg/kg), but there was no significant difference in the percentage of tumor-bearing animals between the treated animals and the untreated controls. Other groups were treated with dimethylnitrosamine (10 mg/kg), benzo(a)pyrene (5 mg/kg), or 3-methylcholanthrene (5 mg/kg), or their combinations with DES. There was no significant difference in tumor frequency between the groups treated with the carcinogens only and those treated with the carcinogens and DES. Solid tumors in the abdominal cavity and hepatic tumor were also found in addition to lung tumors and lymphomas in the DES-treated groups. Other groups were treated with urethane with or without BCG or Escherichia coli endotoxin (ET): the carcinogenic effect of urethane was not modified by BCG and ET. In other experiments, urethane induced multiple lung tumors with and without DES, but the number of lymphomas was significantly higher in the group treated with urethane and DES than in the groups treated with urethane or DES alone. (24 Refs) (In HUN)

47. TUMORIGENICITY OF BAY-REGION DIOL-EPOXIDES AND OTHER BENZO-RING DERIVATIVES OF DIBENZO(A,H)PYRENE AND DIBENZO(A,I)PYRENE ON MOUSE SKIN AND IN NEWBORN MICE.

Chang RL, Levin W, Wood AW, Lehr RE, Kumar S, Yagi H, Jerina DM, Conney AH
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Cancer Res; 42(1):25-29 1982

Dibenzo(a,h)pyrene [DB(a,h)P], dibenzo(a,i)pyrene [DB(a,i)P], and seven of their benzo-ring derivatives were tested for tumorigenic activity on mouse skin and in newborn mice. In the tumor studies on mouse skin, a single topical application of 50, 200, or 600 nmol of compound was followed 7 days later by twice-weekly applications of the tumor promoter 12-O-tetradecanoylphorbol-13-acetate for 16 or 24 wk. With the exception of 2,10-difluorodibenzo(a,i)pyrene, all of the compounds had significant tumor-initiating activity at all doses tested. trans-1,2-Dihydroxy-1,2-dihydrodibenzo(a,h)pyrene and trans-3,4-dihydroxy-3,4-dihydrodibenzo(a,i)pyrene, the metabolic precursors of bay-region diol-epoxides, had tumor-initiating activity that was equivalent to their parent hydrocarbons. Saturation of the double bond in the benzo-ring of these dihydrodiols resulted in the formation of tetrahydrodiols whose tumor-initiating activity was not significantly different from that observed with the corresponding dihydrodiols at the 50-nmol dose. The bay-region diol-epoxides of DB(a,h)P and DB(a,i)P, in which the benzylic hydroxyl group and the oxirane oxygen are trans (Isomer 2), induced significantly fewer tumors per mouse than did their dihydrodiol and parent hydrocarbon precursors. In the tumorigenicity study in newborn mice, a total dose of 87.5 nmol of the hydrocarbon divided into three ip injections was administered on the 1st, 8th, and 15th day of life, and tumorigenic activity was determined when the mice were 49 to 54 wk old. trans-1,2-Dihydroxy-1,2-dihydrodibenzo(a,h)pyrene and trans-3,4-dihydroxy-3,4-dihydrodibenzo(a,i)pyrene induced three- to eight-fold more pulmonary tumors per mouse and four- to five-fold more hepatic tumors per male mouse than the respective parent hydrocarbons. The corresponding tetrahydrodiols had no more than one-eighth of the pulmonary tumorigenic activity of the corresponding dihydrodiol. The bay-region diol-epoxide (Isomer 2) of DB(a,h)P had tumorigenic activity equal to the parent hydrocarbon but significantly less than its dihydrodiol precursor. The bay-region diol-epoxide (Isomer2) of DB(a,i)P was highly toxic, and only 19% of the mice survived to termination of the study. This diol-epoxide had significantly less tumorigenic activity towards the lung than did either its dihydrodiol precursor or the parent hydrocarbon. Notably, 20% of the surviving mice treated with the diol-epoxide of DB(a,i)P had leukemia at the termination of the study. 2,10-Difluorodibenzo(a,i)pyrene had no tumorigenic activity in newborn mice at the single dose tested. These results are discussed in relationship to the bay-region theory of polycyclic aromatic hydrocarbon carcinogenicity. (Author abstract) (27 Refs)

48. GENETIC STUDY OF N-NITROSOMETHYLUREA-INDUCED THYMIC LYMPHOMA IN INBRED MICE (MEETING ABSTRACT).

Mayer A
No affiliation given
Tenth International Symposium for Comparative Research on Leukemia and Related Diseases, August 31-September 4, 1981, Los Angeles, California. 187 pp., 1981.

Mice of various inbred strains were injected ip with the chemical carcinogen N-nitrosomethylurea to induce thymic lymphoma. All the strains developed this specific neoplasia to high incidences, but marked differences were observed between strains with respect to the duration of the latent period, which extended from exposure to the carcinogen at 5-9 wk of age until overt development of thymic lymphoma (indicated by labored breathing) followed shortly thereafter by death. The RF/J and AKR/J strains showed the shortest latent periods, with deaths occurring from 12 to 18 wk of age. The 129 and C57BL/6 strains were characteristic of the longer-latency type, with deaths occurring from 16 to 30 wk of age. In two crosses tested, the AKR x 129 and the 129 X RF, the short-latency phenotype was observed to be dominant. Data from the (129 x RF) F1 x 129 backcross will be presented to indicate the number of loci involved in the short-latency phenotype, and to discern whether endogenous ecotropic murine leukemia virus and/or the H-2 locus plays a role in this phenomenon. (no Refs)

49. MUTAGENIC EFFECT OF TRICHLORFON AND DIMETHOATE ON MOUSE MYELOCYTES IN VIVO.

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Egeszsegtudomany; 25(3):262-266 1981

The mutagenic effects of trichlorfon (TF; 1 x 405 mg/kg ip) and dimethoate (1 x 20 or 1 x 60 mg/kg ip) were studied in male CFLP mice after 24 and 48 hr. Significant differences were found in the number of aberrant cells 24 and 48 hr after treatment with TF, and 24 and 48 hr after treatment with 60 mg/kg dimethoate. The number of aberrant cells 48 hr after TF treatment was 22/200 vs 5/200 in the controls (p less than 0.01). Numerical aberration was found in 1/200 cases (0/200 in the controls), chromatid gap in 21/200 (4/200 in the controls), and break in 0.200 (1/200 in the controls). The number of aberrant cells 48 hr after treatment with 60 mg/kg dimethoate was 51/200 (vs 6/200 in the controls): numerical aberration was found in 7/200 cases (vs 0/200 in the controls), chromatid type aberration in 35 (4 in the controls), and chromosome type aberration (acentric fragment and deletion) in 9 (in the controls). The findings suggest the possibility of the mutagenic effect of both substances. (26 Refs) (In HUN)

EXPERIMENTAL STUDIES: DNA TUMOR VIRUSES

50. ACTIVATION OF EPSTEIN-BARR VIRUS EXPRESSION IN LATENTLY INFECTED HUMAN LYMPHOBLASTOID CELLS WITH BACTERIAL FATTY ACIDS AND PROMOTORS OF PLANT AND MICROBIAL ORIGIN: A POSSIBLE CAUSE FOR BURKITT'S LYMPHOMA AND NASOPHARYNGEAL CARCINOMA (MEETING ABSTRACT).

Ito Y, Kishishita M, Yanase S, Kawanishi M, Takashima M, Imanaka H
No affiliation given
Tenth International Symposium for Comparative Research on Leukemia and Related Diseases, August 31-September 4, 1981, Los Angeles, California. 187 pp., 1981.

When used in combination with 12-O-tetradecanol phorbol-13-acetate (TPA) and/or croton oil, even other common fatty acids like i-butyric acid and propionic acids also exherted marked Epstein-Barr virus (EBV)-inducing activity in nonproducer Raji cells. This led us to test the bacteria-produced short-chain fatty acids as EBV-inducers both with and without promotors and, found that the members of Fusobacterium, Clostridium and other species, those which produce such compounds as their metabolites, indeed play a significant role in the activation of EBV expression as detected by EBV-early (EA) and -viral capsid antigens (VCA). On the other hand, the roots of croton oil, the parent compound of TPA, was traced back to a leafy shrub, Croton tiglium, a plant native to Southeastern Asia. Incidentally, we came across a fact that the seed from which croton oil is expressed has been used as herbal drug in Southern China for over 1000 yr. This prompted us to test other analogous extracts from the Euphorbiaceae family to which C tiglium belongs. The ether extracts prepared from all these Euphorbiacea plants proved to be an efficient EBV-inducers. The Euphorbiacea plants currently used as herbal medicaments amount to more than 30 species in Southern China and as much as 90 in East Africa. We have recently observed that an indol-alkaloid produced by a variant of Streptomyces mediocidius, Teleocidin B, also can act as a powerful inducer and activator of EBV with an efficiency comparable to TPA in our producer and nonproducer test system. (1 Ref)

51. ANALYSIS OF THE TRANSFORMATION OF HUMAN LYMPHOCYTES BY EPSTEIN-BARR VIRUS III. INDUCTION OF EARLY EVENTS BY P3HR-1 STRAIN WITHOUT SUBSEQUENT IMMORTALIZATION.

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Med Microbiol Immunol (Berl); 170(1):19-26 1981

The interaction between Epstein Barr virus (EBV) derived from P3HR-1 cell line and human cord blood lymphocytes was studied by simultaneous observations of events occurring in EBV-induced transformation in individual cells. EBV derived from B95-8 cells (B95-8 EBV) was used for positive control. B95-8 EBV induced a complete series of early transformation events including nuclear antigen (EBNA) and DNA synthesis and blastogenesis, followed by immortalization of the infected lymphocytes. When the same cord preparation was exposed to P3HR-1 EBV, EBNA-positive cells were clearly identified even 12 hr after viral exposure and reached a max of 31% at 24 hr, followed by a plateau for a subsequent 24 hr. In contrast to B95-8 EBV infection, EBNA staining was weak. At 24 hr, blastogenesis was also significant while 3H-thymidine incorporation was not. In addition to weak fluorescence, brilliant EBNA staining later occurred at 48 hr and reached about 20% of the total positive cells on day 5. The EBNA-positive blast cells then became grain-positive at 36 hr and the immunofluorescent cells reached 61.1% at 120 hr. At this time, nearly 50% of the stained nuclei showed evidence of DNA synthesis. At 72 hr, all examined mitotic cells were positive for EBNA and the mitotic frequency was as high as that seen in B95-8 EBV infections. Characteristic cell aggregates were also seen. The number of infected cells decreased gradually after 1 wk and degenerated in about 2 wk. Essentially the same results were obtained, using different stocks of EBV derived from both P3HR-1 sublines A and B and different cord cell preparations. The results indicated that P3HR-1 virus does retain early transforming functions for primary human B lymphocytes, although infected cells have a short life span. (28 Refs)

52. EPSTEIN-BARR VIRUS-SPECIFIED POLYPEPTIDES IN BURKITT LYMPHOMA/SOMATIC CELL HYBRIDS (MEETING ABSTRACT).

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No affiliation given
Tenth International Symposium for Comparative Research on Leukemia and Related Diseases, August 31-September 4, 1981, Los Angeles, California. 187 pp., 1981.

Adding 5'-iododeoxyuridine (IUDR) to cultured Burkitt lymphoma/somatic cell hybrids (D98/HR-1) leads to expression of Epstein-Barr virus (EBV) early antigen (EA). When the drug is removed, the cells synthesize virus DNA, virus capsid antigen (VCA), and ultimately virus particles. The EBV-specified polypeptides present in cells before and after removal of IUDR were immunoprecipitated with serum having high antibody titers against the EBV nuclear antigen (EBNA), EA, and VCA. These polypeptides were then analyzed by sodium dodecyl sulfate-polyacrylamide gel electrophoresis. Their cellular location was determined by isolating nuclear and cytoplasmic fractions from the induced cells prior to radioimmunoprecipitation. The predominant polypetides associated with the synthesis of EA had apparent mol wt of 125 and 82 kilodaltons, respectively. The larger polypeptide was found primarily in the nucleus, whereas the smaller polypeptide was found in both nuclear and cytoplasmic fractions. Two prominent polypeptides having apparent mol wt of 141 and 133 kilodaltons were detected after the initiation of virus DNA synthesis. These appear to be the major components of VCA and may correspond to VP6 and VP7. In addition to these four prominent polypeptides, several additional polypeptides were specifically immunoprecipitated. Preliminary data suggest that the polypeptides immunoprecipitated from induced epithelial hybrid cell are very similar to those present in lymphoblastoid cells. (1 Ref)

53. IDENTIFICATION OF ANTIGENIC DETERMINANTS UNIQUE TO THE SURFACES OF CELLS TRANSFORMED BY EPSTEIN-BARR VIRUS.

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Nature; 294(5840):458-460 1981

Four monoclonal antibodies (anti-EBVCS) that detect antigenic determinants unique to the surfaces of Epstein-Barr virus (EBV)-transformed cells but are not associated with virus production were isolated. Cell lines transformed in vitro or those transformed in vivo but not associated with Burkitt's lymphoma bound anti-EBVCS strongly, whereas cell lines from

patients with Burkitt's lymphoma bound them at intermediate levels or not at all. When untreated lymphocytes and lymphocytes exposed to EBV, Concanavalin A, and pokeweed mitogen were assayed, only EBV-exposed lymphocytes expressed EBVCS determinants, which were detectable within 48 hr after infection. Assay of unseparated populations of EBV-exposed primary lymphocytes and immunoglobulin-positive and -negative populations indicated that those cells which express EBVCS determinants are separated as B cells along with those which express the EBV-induced nuclear antigen and that the two antigen-expressing populations are overlapping and may be identical. A polypeptide with an apparent mol wt of 45,000 was precipitated from an EBVCS-positive cell line and was likely to be the molecule which carries EBVCS determinants. The results indicate that EBVCS determinants are expressed at reduced levels on cell lines established from Burkitt's lymphoma patients relative to expression on other EBV-transformed cell lines. EBVCS determinants are among possible determinants recognized by autochthonous, cytotoxic T cells specific for EBV-transformed cells and may therefore be equivalent to lymphocyte determined membrane antigen (LYDMA); this possibility was supported by the finding that EBVCS and LYDMA were expressed with the same time course in lymphocytes infected with EBV in vitro. If the EBVCS determinants are used by cytotoxic T cells to identify their targets, reduced expression of EBVCS on Burkitt's lymphoma cell lines is consistent with these tumor cells having been selected in vivo to survive that cytotoxic response. (18 Refs)

54. CELL SURFACE COMPONENTS OF HUMAN AND NONHUMAN PRIMATE B AND T LYMPHOCYTES (MEETING ABSTRACT).

Neubauer RH, Levy R, Marchalonis JJ, Strnad BC, Rabin H
No affiliation given
Tenth International Symposium for Comparative Research on Leukemia and Related Diseases, August 31-September 4, 1981, Los Angeles, California. 187 pp., 1981.

Nonhuman primates have been used as experimental models of human lymphoid tumors. These neoplasms can be virally induced or arise spontaneously and have been shown to affect either B or T cell populations. Previous studies have shown that the properties of nonhuman primate lymphoid cells (either fresh lymphocytes or established cell lines) are remarkably similar to those of man. In the present study we extend these comparisons to an analysis of lymphocyte markers as defined by monoclonal antibodies against human RBC antigens and by using heteroantisera to examine immunoglobulin related determinants on B and T cells. The monoclonal antibodies used were specific for T cell, lymphoid, lymphoid:myeloid, and thymus cell antigens plus Ia antigens, and beta 2 microglobulin. The cells examined included B and T lymphoblastoid cell lines established either spontaneously or by viral transformation and fresh peripheral blood lymphocytes separated by sheep RBC rosetting into T cell and non T cell fractions. Results of these studies showed that the antibodies gave complete crossreactivity with gorilla and chimpanzee cells while B cell lines of orangutan origin had lost lymphoid, thymus, and beta 2 microglobulin markers. Gibbon cells and cells of Old World and New World monkeys reacted only with monoclonal antibodies against Ia antigen determinants. These Ia antigens were found on the non T cell fraction of fresh peripheral lymphocytes, on B cell lines and on virus induced T cell tumor cell lines of owl monkey and marmoset origin. Immunoprecipitation analysis using the anti Ia antibodies showed a degree of molecular diversity on owl monkey and marmoset cells compared to the Ia antigens associated with human cells. (no Refs)

EXPERIMENTAL STUDIES: RNA TUMOR VIRUSES

55. EXPERIMENTS WITH CLONED COMPLETE TUMOR-DERIVED BOVINE LEUKEMIA VIRUS INFORMATION PROVE THAT THE VIRUS IS TOTALLY EXOGENOUS TO ITS TARGET ANIMAL SPECIES.

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J Virol; 40(2):605-609 1981

Taking advantage of the existence of a unique SacI restriction site in the long terminal repeats of the integrated bovine leukemia virus proviral DNA isolated from a bovine tumor, the total viral information (about 9.2 kilobases) was cloned in the lambdoid vector lambdaWES.lambdaB. Use of this cloned bovine leukemia virus DNA allowed us, for the first time, to definitely rule out the existence of any endogenous bovine leukemia virus sequence in the bovine, ovine, caprine, murine, feline, chicken, or human genomes. These data prove the absence of acquired cellular information in the provirus that has give n rise to a tumor. (Author abstract) (20 Refs)

56. BIOCHEMICAL AND IMMUNOLOGICAL STUDIES OF THE BOVINE LEUKEMIA VIRUS (BLV) (MEETING ABSTRACT).

Portetelle D, Deschamps J, Kettmann R, Bruck C, Couez D, Mammerickx M, Burny A
No affiliation given
Tenth International Symposium for Comparative Research on Leukemia and Related Diseases, August 31-September 4, 1981, Los Angeles, California. 187 pp., 1981.

Animals infected by BLV (Bovine Leukemia Virus) synthesize antibody (Ab) directed against all BLV structural proteins. Ab to BLV gp51 appear first, their titer increasing regularly until the host's death; they exhibit cytotoxic activity to BLV-producing cells. BLV gp51 was purified to homogeneity and used in radioimmunoassays run in liquid or in mixed solid-liquid phase. These techniques allowed the conclusion that many animal species, ia cattle, sheep, goat, rabbit, monkey are sensitive to BLV and can be experimentally infected. Infection of cattle, sheep and goats can lead to lymphoid tumors; infection of rabbits leads to leukopenia. We have shown that the antigenic site of BLV gp51 reacted against by the infected animal as unique and involved the carbohydrate moiety of the glycoprotein. Genetic variants of BLV were uncovered by restriction analysis of DNA of BLV-infected cells. One of these variants showed a deletion of about 5000 base pairs toward the 5' end of the viral genome. In general, the same cell clone proliferates in all tumors of a given animal. In some cases, tumors of different clonal origin were found in the same animal. The 3' ends of the provirus and flanking sequences found in two such tumors were cloned and sequenced. Data will be presented and discussed. (no Refs)

57. INFECTIVITY AND METHYLATION OF RETROVIRAL GENOMES IS CORRELATED WITH EXPRESSION IN THE ANIMAL.

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Cell; 26(2,part2):221-232 1981

We studied mechanisms controlling gene expression during animal development using retroviruses as model genes. For this, substrains of mice have been previously derived carrying the Moloney leukemia virus (M-MuLV) in their germ line. Virus activation occurs in some of these substrains at different stages of development, resulting in two classes of viral genomes. The genetically transmitted (endogenous) copy is present in every cell, whereas somatically acquired ('exogenous') copies are carried only in cells that were superinfected We compared these two classes of M-MuLV genomes using two parameters. DNA sequences of the endogenous M-MuLV genome in all mouse substrains were highly methylated in GCGC, the recognition sequence of the restriction enzyme Hha I, and were not infectious (specific infectivity less than 10(-7) pfu per proviral genome) in a DNA transfection assay. In contrast, the 'exogenous' copies were hypomethylated and infectious. These parameters are strongly correlated to genome activity in the animal: only tissues carrying exogenous copies express virus-specific RNA. With the assumption that gene expression of transfected DNA is controlled by mechanisms that are relevant for gene expression in the animal, our results suggest that DNA methylation plays a causative role in gene regulation during development and differentiation. (Author abstract) (43 Refs)

58. IMMUNOPREVENTION OF TYPE-C VIRUS-INDUCED MURINE LEUKEMIAS BY VACCINATION WITH VIRAL ENVELOPE POLYPEPTIDES (MEETING ABSTRACT).

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No affiliation given

Tenth International Symposium for Comparative Research on Leukemia and Related Diseases, August 31-September 4, 1981, Los Angeles, California. 187 pp., 1981.

Prevention of virus-induced murine leukemia was attempted by active immunization with subunit vaccines in two different models: erythroleukemia developing in STU mice after experimental injection of Friend virus complex and spontaneous thymic leukemia of AKR mice. Highly purified envelope polypeptides prepared from Friend (FLV)-, AKR- and feline (FeLV) leukemia virus were emulsified in incomplete Freund's adjuvant and used as immunogens. First results showed that 20/20 STU mice immunized with 100 ug of FLV gp85 survived a challenge dose of FLV inducing fatal erythroleukemia in 90-100% of unvaccinated controls, while 3/7 animals receiving 10 ug of FLV gp85 died with leukemia. Smaller doses were either ineffective, as was adjuvant alone, or even shortened the survival time. Immunization with 100 ug of FLV gp71 was inferior to the same dose of gp85, (2/6 mice died after challenge) but was superior to isolated p15E. Only the immune response to glycoprotein 71 seems to reduce mortality and is probably developed more strongly when gp85 is used as immunogen. The internal core protein p30 and adjuvant alone were ineffective as vaccines. (no Refs)

59. RELEVANCE OF ENDOGENOUS TYPE C RETROVIRUS ON M-MSV ONCOGENESIS: EXPRESSION OF ENDOGENOUS M-MULV AND NATURAL ANTIBODY PRODUCTION ASSOCIATED WITH RESISTANCE TO TUMOR INDUCTION (MEETING ABSTRACT).

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No affiliation given

Tenth International Symposium for Comparative Research on Leukemia and Related Diseases, August 31-September 4, 1981, Los Angeles, California. 187 pp., 1981.

Previous work has shown that mice which express high titers of endogenous type C ecotropic retrovirus are partially or totally resistant to tumor induction by Moloney murine sarcoma virus (M-MSV). To further investigate the role of endogenous virus in M-MSV oncogenesis, BALB/Mo mice, which carry the Moloney murine leukemia virus (M-MuLV) as an endogenous, genetically transmitted virus on BALB/ c background, were studied. Groups of BALB/Mo and conventional BALB/c mice were injected im with M-MSV at different ages (3-6 wk). As expected BALB/c mice were fully susceptible to M-MSV tumor induction, and all developed tumors in one wk. On the contrary, in 6 wk old BALB/Mo mice tumors appeared only in 17% of mice and after a prolonged latent period. A certain degree of resistance was also present in 3 wk old BALB/Mo mice as revealed by a longer tumor latency than in age-matched BALB/c mice. To elucidate the possible mechanisms underlying the resistance, BALB/Mo mice were tested for M-MuLV expression at different ages by the UV-XC plaque test. It was found that tumor resistance paralleled the time course of M-MuLV activation since mice became virus positive starting at 2 wk of age and all mice were positive at 8 wk. Furthermore, normal BALB/Mo sera tested for antibody production against M-MuLV surface determinants, using a 125I-protein A binding assay, disclosed a relevant degree of binding capacity already present in some 3-4 wk old individuals and which increased further with age. An additional study carried out in female BALB/J x male (BALB/J x BALB/Mo) Bcl hybrids also showed a closely correlated pattern between M-MuLV expression, antibody production and M-MSV tumor resistance. (1 Ref)

60. T CELL TOLERANCE AND TUMOR PROGRESSION INDUCED BY THE NEONATAL INJECTION OF MOLONEY MURINE LEUKEMIA VIRUS (MEETING ABSTRACT).

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No affiliation given

Tenth International Symposium for Comparative Research on Leukemia and Related Diseases, August 31-September 4, 1981, Los Angeles, California. 187 pp., 1981.

Tumors induced by Moloney Murine Sarcoma Virus (M-MSV) evolve rapidly at the site of inoculation but undergo spontaneous regression in immunocompetent hosts. This phenomenon has been shown to depend mostly on T lymphocyte reactivity. However, in mice injected neonatally with Moloney Murine Leukemia Virus (M-MuLV-carrier mice) we have found that the resulting tumors did not regress and cytolytic T lymphocytes (CTL) were not generated in vitro. Since M-MuLV and M-MSV possess common antigens, these findings suggest that the T lymphocytes were tolerized following the introduction of the virus at an early stage of development. In fact, we observed that both T and B lymphocytes from carrier mice expressed M-MuLV-induced cell surface antigens as early as a few days after neonatal virus injection. The unresponsiveness observed in these mice cannot be ascribed to the presence

of suppressor cells since cell mixing experiments indicated that spleen cells from progressor mice did not inhibit the generation of M-MSV immune cytolytic T lymphocytes either in vivo or in vitro. In addition, by using a limiting-dilution system to obtain CTL clones specific for M-MuLV cell surface antigens, we observed that the frequency of CTL clones i n M-MuLV carrier mice was very low compared to the frequency determined for normal mice. Finally, following intrathymic injection of M-MuLV in adult mice, we observed that a subpopulation of T lymphocytes in the spleen and lymph nodes expressed virus-induced cell surface antigens, and that autoreactive, virus-specific CTL were generated. (no Refs)

61. INCIDENCE AND PHENOTYPIC HETEROGENEITY OF MOLONEY VIRUS-INDUCED LEUKEMIAS: A MULTIGENIC CONTROL.

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Blood Cells; 7(2):301-311 1981

Adults of seven inbred mouse strains were inoculated with Moloney leukemia virus (MuLV). Incidence of viremia after 2 mo ranged from 1.8% in B6 to 87% in BALB/c while incidence of leukemia after 6 mo ranged from 0% in NZB and DBA/2 to 97% in BALB/c. In individual mice, the host-virus relationship was studied further as to degree of viremia, appearance of leukemia, organ involvement, and surface phenotype of leukemic cells. The viremia was controlled by H-2 and non-H-2 genes. Three of the H-2 genes in the I and D or T region of the major histocompatibility complex (MHC) behave like immune-response genes which control the specific antiviral immune response. Other gene(s) outside the MHC also affected virus production. Both sets influenced leukemia incidence, since leukemias occurred only in highly viremic strains. Additional non-H-2 genes not involved in viremia, were determinants in induction of malignancies, since some sensitive strains did not become leukemic despite high levels of virus. The anatomical type of MuLV-induced leukemias varied according to the non-H-2 background. As an example, most leukemias in B10 congeneic mice involved thymus and were frequently limited to this organ, whereas BALB mice preferentially developed splenic leukemias. In a given strain, leukemias arising in different individuals frequently expressed different phenotypes. It is concluded that MuLV-induced leukemia is a multistep process in which virus production is necessary, but is not sufficient in itself, to induce malignant transformation. (20 Refs)

62. IN VITRO STUDIES ON THE MECHANISM OF LEUKEMOGENESIS (MEETING ABSTRACT).

Yokoro K, Yanagihara K, Hamada K, Imamura N, Kodama Y, Kajitani T, Kamiya K, Seyama T
No affiliation given
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Seven thymic epithelial reticulum (TER) cell lines were established from thymuses of a 2 mo-old, a 6 mo-old, two spontaneously leukemic AKR/Ms mice, two x-ray-induced leukemic C57BL/6N mice and a 2 mo-old NFS/N mouse. Numerous type-C virus particles with the occasional budding form were observed i n all but one cell lines. Normal thymocytes cocultivated with TER monolayers were transplanted into pre-irradiated syngeneic mice to examine the leukemogenic potential of TER cells. Neither acceleration nor development of leukemia was observed in the recipient mice. TER celll lines were established from thymuses of a 2 mo-old (A2T), a preleukemic 6 mo-old (A6T) and two lymphoma-bearing (ASLT-1 and ASLT-2) AKR/Ms mice. Expression of XC-detectable N-tropic ecotropic virus was observed in every cell line, while the presence of xenotropic and MCF-type viruses could be detected only in TER cells derived from preleukemic and leukemic mice. Expression of xenotropic virus in various cells of newborn and young AKR mice of up to 3 mo of age could readily be induced by iododeoxyuridine (IdUrd) treatment, while MCF virus was never detected in these cells, with an important exception that MCF virus with dual-tropic infectivity emerged in addition to ecotropic and xenotropic viruses in A2T cell line of more than 20 passages. These spontaneously-emerging and IdUrd-induced MCF viruses were purified and their virological properties were characterized. The cloned MCF viruses (MCFs AT1, AT2, AT3 and AT4-IU) showed dual-tropism and produced CPE-like foci on mink lung cells. Spontaneous leukemogenesis in AKR mice was effectively accelerated by the neonatal inoculation of MCF viruses, but not by the inoculation of either ecotropic or xenotropic virus. (no Refs)

63. ABELSON VIRUS-INFECTED CELLS CAN EXHIBIT RESTRICTED IN VITRO GROWTH AND LOW ONCOGENIC POTENTIAL.

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J Virol; 40(2):577-584 1981

We have designed a method for growing bone marrow cells infected with Abelson murine leukemia virus which permits examination of target cell growth early after infection. This culture system increases the efficiency of target cell growth by favoring rapid growth of a mixed population of adherent cells in the primary culture. the nonadherent Abelson virus-infected cell populations expressed pre-B-cell differentiation markers characteristic of Abelson virus-transformed cells (mu-heavy chains of Ig M and terminal deoxynucleotidyltransferase). Early after infection, these cell populations exhibited restricted in vitro and in vivo growth properties which differed from those of an established Abelson virus-transformed cell line, 2M3. These included a marked dependency upon the adherent cell layer for growth and viability, a lower efficiency of agar colony formation, and a lower capacity for tumor production in syngeneic animals. Growth of the early populations could be maintained in the absence of the adherent cell layer by using conditioned medium from long-term adherent cell cultures established in the absence of viral infection. After passage of the populations for several wk, the in vitro growth properties gradually shifted toward that of the 2M3 cell line. Twelve-wk-old populations grew independently of the adherent cell layer and showed an increased efficiency of agar colony formation. These data indicate that many lymphoid target cells exhibit an intermediate transformed phenotype when infected with Abelson virus. Growth of these cells in culture is mediated via a synergistic interaction between intracellular expression of the viral transforming gene and an exogenous growth-promoting activity which can be provided by cultures of adherent bone marrow cells. (Author abstract) (31 Refs)

64. ISOLATION OF TWO VARIANTS OF DUAL ECOTROPIC AND XENOTROPIC RETROVIRUS FROM THYMUSES OF MICE INOCULATED AS NEWBORNS WITH GROSS PASSAGE A LEUKEMIA VIRUS (MEETING ABSTRACT).

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No affiliation given
Tenth International Symposium for Comparative Research on Leukemia and Related Diseases, August 31-September 4, 1981, Los Angeles, California. 187 pp., 1981.

Two variants of dual ecotropic and xenotropic Retrovirus were isolated from thymuses of C3HeB/Fe mice inoculated as newborns with Gross Passage A leukemia virus (GPAV). The first variant, Th2P1, was isolated from a mouse having definite leukemic symptoms and the second, Th4P1, was from a mouse in preleukemic phase without leukemic symptoms. Both viruses replicated as efficiently in mink cells as in mouse cells, for which they showed the same N tropism as GPAV. They did not trigger formation of syncytium in XC tests. Th2P1 virus induced foci of cytopathic effect in mink cells. Th4P1 virus possessed helper activities vis-a-vis both S+L- mink and S+L- mouse cells and was neutralized significantly not only by anti-xenotropic virus serum but also by anti-ecotropic virus serum. Both viruses were devoid of leukemogenic activity when inoculated into susceptible newborn mice. However, they accelerated significantly appearance of leukemia in GPAV infected C3HeB/Fe mice as well as in AKR mice. Recombinants between exogenous ecotropic GPAVs and activated endogenous xenotropic viruses were postulated. (no Refs)

65. THE TRANSFORMING SEQUENCES OF AVIAN MYELOCYTOMATOSIS VIRUS (MC29).

Lautenberger JA, Schulz RA, Garon CF, Tsichlis PN, Spyropoulos DD, Pry TW, Rushlow K, Papas TS
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J Supramol Struct Cell Biochem; 16(2):193-207 1981

Avian myelocytomatosis virus (MC29) was isolated and characterized by recombinant DNA methods. DNA was obtained from the transformed nonproducer quail cell line Q5. This DNA was cloned using a library of phage prepared from a size-fractionated digest of Q5 DNA. Cloned DNA was then analyzed by Southern blotting of endonuclease digests and electron microscope examination of loops formed between the DNA and RNA from MC29 or helper virus. Cloned DNA consisted of approx 9.2 kilobases (kb), including approx 4 kb of viral DNA and 5.2 kb of quail cell DNA. The MC29-specific sequences, 5' helper-related sequences, and part of the envelop region were included in the viral portion. A cloned EcoRI fragment corresponded to the major band of EcoRI-cleaved DNA from Q5 cells that hybridized to viral sequences. Cloned DNA produced foci of transformed cells with high efficiency when transfected into NIH 3T3 cells, indicating that the MC29 sequences were functional. (31 Refs)

66. TUMOR ASSOCIATED ANTIGENS AND TRANSFORMATION PROTEINS OF FELINE RETROVIRUSES (MEETING ABSTRACT).

Essex M, Chen AP, Mikami T
No affiliation given
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Cats naturally exposed to feline leukemia virus (FeLV) or feline sarcoma virus (FeSV) mount a humoral antibody response that is directed to tumor associated antigens. Antigens thus far identified as targets for this immunosurveillance-correlated response that are distinct from the virion structural proteins include an antigen of about 70,000 daltons on lymphoid tumor cells (FOCMA-L) and a polyprotein of 84,000 daltons or 110,000 daltons, depending on the strain of virus, on FeSV-transformed fibroblasts. Healthy cats that are exposed to FeLV under natural conditions in leukemia cluster households develop high titers of humoral antibodies to FOCMA. Both adult and young cats that are introduced to such FeLV-exposure environments usually seroconvert to develop FOCMA antibodies within a few mo. When all FeLV-excretor cats are removed from such environments no additional seroconversions occur. However, cats that already have significant humoral antibody titers at the time FeLV-excretor cats are removed maintain humoral antibody titers without re-exposure to FeLV for at least several yr. This suggests that such cats either maintain FeLV in a latent, but not a widely dispersed or excreted form, or that such cats harbor a population of FeLV-altered FOCMA positive cells that are maintained at low levels by an immunosurveillance response. The antigen found in fibroblasts transformed with FeSV is representative of a class of 'gag-x' proteins which are typical of many defective transforming retroviruses in that they contain gag peptides linked to a transformation specific portion designated 'x'. The 'x' portion is encoded by 'one' or 'fes', a member of the set of highly conserved cell genes that become inserted into replication defective retroviruses when they acquire the ability to transform fibroblasts in vitro. Cats inoculated with their own FeSV-transformed cells following in vitro cultivation and transformation develop a humoral antibody response to 'x' of 'ga g-x', as do some highly immune cats that have apparently only been exposed to FeLV. When FeSV is used to induce widely different types of tumors, such as melanomas of neuroectodermal origin and fibrosarcomas of mesodermal origin, the same 'gag-x' is expressed concordantly with the malignant phenotype. (3 Refs)

67. FELINE LEUKEMIA VIRUS-INDUCED ERYTHROID APLASIA: IN VITRO HEMOPOIETIC CULTURE STUDIES.

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Exp Hematol; 9(10):990-1001 1981

Colony forming unit (CFU) assays were developed for feline granulocyte-macrophage (CFUGM), early erythroid (Day 2 CFUE), and late erythroid (Day 7 CFUE) colonies in methylcellulose medium. Feline CFUGM and both Day 2 and Day 7 CFUE were enhanced by feline macrophage conditioned medium and late CFUE often were intimately associated with macrophages. Kittens were inoculated with the Kawakami-Theilen (KT) strain of feline leukemia virus (FeLV) and sequential changes in marrow CFU determined. Erythroid aplasia, characterized by progressive non-regenerative anemia, lymphopenia, and a profound decrease in early and late CFUE but not CFUGM was induced by 3 to 5 wk after FeLV-KT inoculation. The susceptibility of kittens to FeLV-induced erythroid aplasia was strongly age-related; neonatal kittens were most sensitive and substantial natural resistance developed by 4 wk of age. The results demonstrate that FeLV-KT infection induced a rapid and selective suppression of erythroid progenitor cells and represents a suitable model of experimentally-induced acquired erythroid apiasia. (Author abstract) (54 Refs)

68. UNIQUE AND CROSS REACTING ANTIGENS OF FELINE LEUKEMIAS (MEETING ABSTRACT).

Grant CK, Michalek MT
No affiliation given
Tenth International Symposium for Comparative Research on Leukemia and Related Diseases, August 31-September 4, 1981, Los Angeles, California. 187 pp., 1981.

Following exposure to feline leukemia virus (FeLV) cats that resist leukemia produce complement dependent antibodies (CDA). These antibodies are directed to feline oncornavirus associated cell membrane antigen (FOCMA) found on the surface of most feline leukemias. To determine the CDA-defined cross reactivity of FOCMA on feline leukemias, five individual FeLV producing tumor lines (FL74, F422, 3272, 3281, and 79-14940) were compared. The cytotoxic profiles to the leukemia target lines were determined for 147 sera from FeLV exposed cats, and animals were identified whose sera would selectively lyse almost any possible combination of tumors from one to all five lines tested. Cross absorption and cold target inhibition studies were performed on selected sera and a spectrum of different antigens was identified which included both individual determinants and antigens shared by some of the tumor lines. Leukemias FL74 and F422 carried a cross-reactive determinant which was distinct from a second antigen shared by 3272 and 3281; lines F422, 3272, and 3281 each also carried a unique antigen. Determinants present on leukemia line 79-14940 did not cross-react with those found on the other cell lines. In as much as CDA was removed by absorption with normal cells from some cats, it is possible that the targets of CDA mediated lysis on leukemia cells may be associated with feline histocompatibility antigens. Information will be presented concerning the nature of the leukemia antigens, and the role that multiple FOCMA determinants might play in leukemia immunity and tumor escape. (no Refs)

69. FRIEND VIRUS TRANSFORMED CELLS IN THE ADVANCED STAGES OF ERYTHROLEUKEMIA.

Mager DL
University of Toronto, Toronto, Canada
Diss Abstr Int [B]; 42(3):886-B 1981

Friend erythroleukemia appears to consist of an early 'preleukemic' phase and a later phase in which truly leukemic or tumorigenic cells appear. Although the early stage of the disease, characterized by splenomegaly and erythroblastosis, has been extensively studied, relatively little is known about the late malignant stage of Friend erythroleukemia. The primary aim of this work was to develop procedures for the detection and characterization of the leukemic cells emerging in the advanced stages of erythroleukemia induced by two distinct strains of Friend leukemia virus. An in vitro colony method has been developed which appears to detect a class of malignant Friend virus-transformed cells specific to the advanced stages of erythroleukemia. This method detects cells, capable of forming macroscopic colonies in methylcellulose, which appear in the spleens of mice late after infection with the anemia-inducing (FV-A) or polycythemia-inducing (FV-P) strain of Friend virus. The progeny of these colony-forming cells produce Friend virus, are capable of forming spleen colonies in irradiated syngeneic hosts, are tumorigenic, and can be established as permanent erythroid cell lines. An in vivo spleen colony method has also been developed that detects a class of cells appearing late after infection with Friend virus. These cells are able to proliferate to form macroscopic spleen colonies in irradiated S1/S1d mice. Mice of this genotype have a defective cellular microenvironment that prevents spleen colony formation by normal hemopoietic stem cells. Thus, these observations form the basis of the first in vivo colony assay for Friend virus transformed cells and demonstrate that these cells have become at least partially independent of a normal cellular regulatory factor. (no Refs)

70. CLONAL ANALYSIS OF EARLY AND LATE STAGES OF ERYTHROLEUKEMIA INDUCED BY MOLECULAR CLONES OF INTEGRATED SPLEEN FOCUS-FORMING VIRUS.

Yamamoto Y, Gamble CL, Clark SP, Joyner A, Shibuya T, MacDonald ME, Mager D, Bernstein A, Mak TW
Ontario Cancer Inst., 500 Sherbourne St., Toronto, Ontario, Canada M4X 1K9
Proc Natl Acad Sci USA; 78(11,part2):6893-6897 1981

The integrated proviral DNA of the polycythemia-inducing isolate of Friend spleen focus-forming virus (SFFVP) has been identified in rat cell clones nonproductively infected with this replication-defective erythroleukemia virus and cloned in phage lambda vectors. These lambdaSFFVP recombinants, lambdaSFFVP502 and lambdaSFFVP542, contain endonuclease EcoRI inserts of size 7.4 and 8.2 kilobases, respectively, and include full copies of the SFFVP genome, along with host flanking sequences. Infectivity of the cloned SFFVP genomes was tested by a two-step DNA transfer procedure involving transfection of the cloned DNA into 3T3 mouse fibroblasts or cotransfer of the cloned DNA into thymidine kinase-deficient 3T3 cells together with the cloned thymidine kinase gene of herpes simplex virus, followed by rescue of the transferred DNA by superinfection with a helper virus. Inoculation of the rescued virus into adult mice resulted in the appearance of spleen foci, rapid splenomegaly, and polycythemia. Early after infection, spleen cell populations contained large numbers of cells capable of forming small erythroid colonies in vitro (CFU-E) in the absence of erythropoietin. Late after infection, these mice contained cells capable of forming macroscopic colonies (CFU-FV) in vitro. These data indicate that molecular clones of SFFVP, in conjunction with a helper virus, induce the appearance of hemopoietic colony-forming cells characteristic of both the early and late stages of Friend leukemia. (Author abstract) (35 Refs)

REVIEWS AND OTHER RELATED STUDIES

71. ONCOGENIC VIRUSES.

Wyke JA
Imperial Cancer Res. Fund, P.O. Box 123, Lincoln's Inn Fields, London WC2A 3PX, England
J Pathol; 135(1):39-85 1981

Virus-induced cancer in animals, including man, and the molecular mechanisms of virus-induced neoplasia are reviewed. Topics discussed include the diversity of relationships between oncogenic viruses and host animals, the problem of identifying human tumor viruses, and a brief catalogue of clinically important oncogenic viruses (avian retroviruses, murine leukemia and sarcoma viruses, leukemia and sarcoma viruses of other species, mouse mammary tumor virus, retroviruses and non-neoplastic disease, papovaviruses, adenoviruses, lymphotropic herpesviruses, other herpesviruses, hepatitis B virus, and poxviruses). General features of the interactions between viruses and their host cells, the transformed cell, replication of retroviruses, and cell transformation and tumor formation by retroviruses are discussed. (85 Refs)

72. LEUKEMIA REVISITED.

Cronkite EP, Gallo R. Sachs L, BessisM, Greaves MJ, Shohet SB, Lajtha L, Brecher G, McCulloch EA, Jasmin C
Medical Dept., Brookhaven Natl. Lab., Upton, NY, 11973
Blood Cells; 7(1):11-30 1981

A historical review of the growth of medical understanding of leukemia is presented. Leukemic cell proliferation has been studied by autoradiography of DNA-labelled cells and by various newer cell-culture methods; the information from these studies are compared. It is suggested that adequate clinical trials of tritiated thymidine and extracorporeal radiation as treatment modalities be undertaken. (65 Refs)

73. BLAST CELLS IN ACUTE MYELOBLASTIC LEUKEMIA: A MODEL.

McCulloch EA, Till JE, Ross D, Jasmin C, Brecher G, Cronkite EP
Ontario Cancer Inst., 500 Sherbourne St., Toronto, Ontario M4X 1K9, Canadad
Blood Cells; 7(1):63-77 1981

The literature is reviewed to arrive at a model of the origin and evolution of acute myeloblastic leukemia (AML) as a clonal hemopathy. The model is summarized by the following assumptions derived from the review: determination of a pluripotent stem cell to a leukemic clone occurs abruptly (intermediate stem cell classes are rare); differentiation is unidirectional with no reversal even in anaplastic cancers (clonal maintenance is by stem cell renewal); abnormal clones originate in pluripotent hemopoietic stem cells: transformed committed progenitors are not self-maintaining; the biological properties of abnormal clones include clonal dominance, clonal suppression, and genetic variability; AML originates by genetic transformation in pluripotent stem cells; transformed stem cells give rise to AML blast-cell populations through events analogous to those involved in determination, producing a lineage independent of myelopoietic differentiation; and AML clones change with time as a result both of environmental and of genetic changes, which influence the capacity for poietic differentiation. (47 Refs)

74. CURRENT CONCEPTS ON THE AETIOPATHOGENESIS OF ACUTE LEUKAEMIA.

Torres A, Martinez Guibelalde F, Gomez Garcia P, Garcia Castellano JM, Manzanares Escribano MR
Jefe Servicio Hematologia, Ciudad Sanitaria 'Reina Sofia' de la Seguridad Social, Cordoba, Spain
Sangre (Barc); 26(5B):700-717 1981

A review is presented on the etiological factors presumably or actually involved in the genesis of acute leukemia, attempting a conceptual approach to the mechanisms of leukemogenesis. viral, physical, chemical, and genetic factors are analyzed along with the alleged influence of the regulators of hemopoiesis and the role they may play in the expression, consolidation, and development of the acute leukemias. (Author abstract) (152 Refs) (In SPA)

75. THE LYMPHOMAS, LYMPHADENOPATHY, AND HISTIOCYTOSES.

Murphy SB
St. Jude Children's Res. Hosp., Memphis, TN
Hematology of Infancy and Childhood Volume II. Nathan DG and Oski FA, ed. Philad elphia, W. B. Saunders Company, 774 pp., 1981.

Epidemiology and incidence, etiology, histopathology, clinical presentations, laboratory findings, staging, treatment, complications, and prognosis of Hodgkin's disease (HD) are reviewed. Non-Hodgkin's lymphoma, (all primary malignancies of lymphoreticular tissue not classified as HD), are discussed separately from HD because of important differences in the neoplastic cells of origin, clinical behavior, and management of the disorder. Pseudolymphomas, non-neoplastic lymphadenopathy, and histiocytic syndromes are presented. (264 Refs)

76. EPIDEMIOLOGY OF CANCER IN CHILDHOOD.

Li FP, Bader JL
Sidney Farber Cancer Center, Boston, MA
Hematology of Infancy and Childhood Volume II. Nathan DG and Oski FA, ed. Philadelphia, W. B. Saunders Company, 774 pp., 1981.

The incidence of malignant neoplasms in children less than 15 yr old in the United States is discussed. Of 7,168 new cases reported in 1970, leukemia was the most frequently occurring cancer (2,357) followed by tumors of the CNS (1417), lymphoma (787), neuroblastoma (540), soft tissue sarcoma (463), Wilms' tumor (450), bone tumor (323), retinoblastoma (197), liver tumor (100), ovarian tumor (77), testicular tumor (57), and others (40%). Cancer risk factors discussed are the environmental carcinogens ionizing radiation, drugs, chemicals, and infectious agents. Host susceptibility includes single-gene diseases, chromosomal disorders, familial cancers, and cancer and birth defects. (288 Refs)

77. GENERAL MECHANISM FOR THE ORIGIN OF LEUKEMIA (MEETING ABSTRACT).

Pillow M, Bendix S
No affiliation given
Tenth International Symposium for Comparative Research on Leukemia and Related Diseases, August 31-September 4, 1981, Los Angeles, California. 187 pp., 1981.

A postulated mechanism for carcinogenesis is applied to virus-induced leukemia and to leukemia caused by radiation and chemical carcinogens. Malignant disease is postulated to be the result of the uncontrolled and inappropriate expression of developmental gene sequences. This inappropriate expression of developmental sequences can be brought about by DNA mutations, caused by radiation or chemical carcinogens, or by oncogenic viruses, which turn on developmental sequences as a part of their mechanism of making progeny virus. When the expression of embryonic or developmental gene sequences is not controlled, clinical neoplasia is the result. In murine leukemia experiments done by Leiberman and Sachs, certain clones of spontaneous leukemic cells were induced to differentiate by normal macrophage and granulocyte-inducing protein (MGI). Inducible clones had increased production of progeny virus as they differentiated by a factor of five to ten. Those clones which, after the MGI treatment, differentiated into completely mature cells, entirely ceased virus production once they were mature. MGI did not affect virus production in erythroleukemic cells, and erythropoietin did not affect virus production in the myeloid leukemic cells. Studies by Fialkow and others indicate that human leukemia is clonal, and that in the terminal stages of the disease virtually all the blood cells are from the neoplastic clone. Further, these studies show that, at least in chronic myelogenous leukemia, the circulating RBC are from the same clone, but do not show the malignant characteristics. Similarly, in polycythemia vera the WBC from the same neoplastic clone are not themselves malignant. Apparently the initial event leading to malignancy can occur earlier in the developmental pathway than the stage of the proliferating neoplastic cells. Non-malignant cells descend from the same ancestor cell which produced the neoplastic clone. Leukemic transformation

seems to relate, in both of these systems, to one or a few developmental steps in a single line of development, even when the original cell in which the lesion occurred was capable of several different lines of development. (2 Refs)

* U. S. GOVERNMENT PRINTING OFFICE: 1962—361-847/114

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1. NUTRITION AND ENVIRONMENTAL HEALTH: THE INFLUENCE OF NUTRITIONAL STATUS ON POLLUTANT TOXICITY AND CARCINOGENICITY. VOLUME 2: MINERALS AND MACRONUTRIENTS.

Calabrese EJ

Environmental Health Program, Div. Public Health, Univ. Massachusetts, Amherst, MA

Nutrition and Environmental Health: The Influence of Nutritional Status on Pollu tant Toxicity and Carcinogenicity. Volume 2: Minerals and Macronutrients. New York, John Wiley and Sons, 468 pp., 1981.

EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

2. RETROSPECT AND PROSPECT OF STUDIES ON DIGESTIVE SYSTEM DISEASES IN CHINA.

Zhang X

Dept. Internal Medicine, Capital Hosp., Chinese Acad. Medical Sciences, Beijing, People's Republic of China

Zhonghua Xiaohua Zazhi; 1(1):1-4 1981

In CHI

3. EPIDEMIOLOGY OF PITUITARY ADENOMAS.

Gold EB

Dept. Epidemiology, Sch. Hygiene and Public Health, Johns Hopkins Univ., 615 Wolfe St., Baltimore, MD, 21205

Epidemiol Rev; 3:163-183 1981

4. BLADDER CANCER EPIDEMIOLOGY.

Matanoski GM, Elliott EA

Dept. Epidemiology, Sch. Hygiene and Public Health, Johns Hopkins Univ., 615 North Wolfe St., Baltimore, MD, 21205

Epidemiol Rev; 3:203-229 1981

5. THE EPIDEMIOLOGY OF BENIGN BREAST DISEASE.

Ernster VL

Dept. Epidemiology and International Health, 1699HSW, Univ. California, San Francisco, CA, 94143

Epidemiol Rev; 3:184-202 1981

ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN CARCINOGENESIS

6. AIR POLLUTION AND BIOLOGICAL DEFENCE.

Schlipkoter HW, Dolgner R

Med. Institut fur Umwelthygiene an der Univ., Gurlittstrasse 53, D-4000 Dusseldorf 1, W. Germany

Zentralbl Bakteriol [Orig A]; 172(4/5):299-311 1981

In GER

7. CANCER AND THE PHYSICOCHEMICAL QUALITY OF DRINKING WATER IN QUEBEC.

Thouez JP, Beauchamp Y, Simard A

Dept. Geography, Univ. Montreal, Montreal, Quebec, Canada

Soc Sci Med [Med Geogr]; 15(1):213-223 1981

VIRAL AND IMMUNOLOGICAL ASPECTS OF CARCINOGENESIS

8. ONCOGENIC VIRUSES.

Wyke JA

Imperial Cancer Res. Fund, P.O. Box 123, Lincoln's Inn Fields, London WC2A 3PX, England

J Pathol; 135(1):39-85 1981

9. ROLE OF VIRUSES IN THE ETIOLOGY OF NATURALLY OCCURRING FELINE LEUKEMIA.

Essex M, Grant CK, Cotter SM, Hardy Jr WD

Dept. Microbiology, Harvard Sch. Public Health, 665 Huntington Ave., Boston, MA, 02115

Haematol Blood Transfus; 26:483-487 1981

METHODOLOGY IN CARCINOGENESIS RESEARCH

10. MAMMALIAN IN VIVO AND IN VITRO CYTOGENETIC ASAYS: A REPORT OF THE U.S. EPA'S GENE-TOX PROGRAM.

Preston RJ, Au W, Bender MA, Brewen JG, Carrano AV, Heddle JA, McFee AF, Wolff S, Wassom JS

Biology Div., Oak Ridge Natl. Lab., Oak Ridge, TN, 37830

Mutat Res; 87(2):143-188 1981

11. BACTERIAL SYSTEMS FOR CARCINOGENICITY TESTING.

Mohn GR

Dept. Radiation Genetics and Chemical Mutagenesis, State Univ. Leiden, Wassenaarseweg 72, 2333 AL Leiden, The Netherlands

Mutat Res; 87(2):191-210 1981

12. MUTAGENESIS BY CHEMICAL AGENTS IN V79 CHINESE HAMSTER CELLS: A REVIEW AND ANALYSIS OF THE LITERATURE.

Bradley MO, Bhuyan B, Francis MC, Langenbach R, Peterson A, Huberman E

Merck Inst. for Therapeutic Res., West Point, PA, 19486

Mutat Res; 87(2):81-142 1981

OTHER REVIEWS IN CARCINOGENESIS

13. CANCER BIOLOGY.

Ruddon RW

Biological Markers Program, NCI-Frederick Cancer Res. Center, Frederick, MD

Cancer Biology. New York, Oxford University Press, 344 pp., 1981.

14. AVOIDABLE CANCER: ATTRIBUTION OF RISK.

Doll R

Radcliffe Infirmary, Oxford, England

S Afr Cancer Bull; 25(3):125-146 1981

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EPIDEMIOLOGY AND ETIOLOGY OF HUMAN LYMPHORETICULAR MALIGNANCIES: OTHER STUDIES

1. THE MORTALITY EXPERIENCE OF ARMY WORLD WAR II CHEMICAL PROCESSING COMPANIES.

Norman JE, Robinette CD, Fraumeni JF
Medical Follow-up Agency, Natl. Res. Council, 2101 Constitution Ave., Washington, DC, 20418
JOM; 23(12):818-822 1981

Tetrachloroethane was used by the Army during World War II in the impregnation of clothing for protection against mustard gas. Thirty-nine chemical processing companies were formed: 10 used tetrachloroethane as a solvent for the clothing impregnite and the remainder used a water solvent proce ss. An age-specific analysis of mortality in relation to race, rank, and military occupational specialty (MOS) was performed in which observed numbers of deaths from principal cause groups were compared with those expected according to US standard mortality rates. Overall cancer mortality for 1,099 white males with tetrachloroethane exposure was 1.26 times that of 1,319 men not involved in the impregnation process. The risks for leukemia, lymphoma, and cancers of the genital organs were moderately elevated, but the numbers were small and no significant excesses were observed. (Author abstract) (17 Refs)

2. DOSIMETRY OF THE ATOMIC BOMB SURVIVORS.

Sinclair WK, Failla P, Bond VP, Loewe WE, Kerr GD, Auxier J, Wyckoff OH, Maruyama T, Schull JW, Land EC, Dobson LR, Mays WC, Seymour J
Argonne Natl. Lab., 9700 South Cass Ave., Argonne, IL, 60439
Radiat Res; 88(3):437-447 1981

A summary of information presented at the Late Effects Workshop on Dosimetry of the Atomic Bomb Survivors was compiled. The relevance of findings obtained on Japanese atomic bomb survivors for the determination of radiation risk estimates is discussed through a review of the history, status and implications of the dosimetry of the survivors. In a study of the radiobiological significance of the HIroshima/Nagasaki data, it was determined that there are qualitative differences between the two cities which suggest the presence of a high-linear energy transfer component at Hiroshima. These include the shapes of the curves for chromosomal aberrations and a difference in the spectrum of leukemia types in the two cities. In another presentation, it was suggested that for Hiroshima, at 2 kilometers, the T65 neutron doses were 9x too high, and the gamma doses 4x too low; the uncertainties (approx a factor of 2) in these estimates can be reduced by additional effort. Another presentation reviewed problems associated with calculating dosimetry for the Japanese atomic bomb survivors. The Ichiban studies showed that the sulfur-activation data from Hiroshima and Nagasaki were in reasonable agreement with T65 doses. The difficulty in correlating the chromosome aberration results found in the two cities with the doses predicted by new calculations is considered. The role of the National Council on Radiation Protection and Measurements in Hiroshima and Nagasaki dosimetry is discussed. Primary points brought out in discussions associated with the symposium are listed. (7 Refs)

3. CARCINOGENIC, MUTAGENIC, TERATOGENIC WORKSHOP.

Suit H, Hall E, Frei E
Dept. Radiation Medicine, Massachusetts General Hosp., Boston, MA, 02114
Cancer Clin Trials; 4(Suppl):37-41 1981

Studies on the incidence of tumors attributed to radiation and chemotherapy are reviewed. An analysis of 106,074 patients receiving radiation therapy between 1958 and 1980 revealed 30 s arcomas which had developed within the irradiated tissue. The median lag period was 10 yr. Of the 30 patients, seven were alive 1.5-20 yr after treatment of the 'radiation-induced' tumor. In patients treated for ovarian carcinoma by alkylating agents, a 15-fold increase in the risk of acute myelogenous leukemia has been reported. Among 438 patients treated for Hodgkin's disease, the observed to expected ratio of leukemia was 3.8 for patients treated with total nodal or extended field radiation therapy, 3.2 for chemotherapy, 23 for extensive radiation and chemotherapy, and 1.6 for local field irradiation. In another study of leukemic development among 1,096 patients treated for Hodgkin's disease, the incidence was 0/417, radiation alone; 12/453, radiation and chemotherapy; 1/124, radiation failure followed by chemotherapy; and 2/37, chemotherapy only. The importance of considering the carcinogenicity of chemotherapeutic agents in future clinical trials is stressed. Models of carcinogenesis include various interpretations of the role of the processes of initiation and promotion. Problems of extrapolation of carcinogenic findings from one model system do another (particularly to humans) include the time distribution of expression of the events, differences in experimental protocols, and variations among cell systems. (no Refs)

4. EPIDEMIOLOGY OF LYMPHOID MALIGNANCY. AN ETIOLOGICAL HYPOTHESIS OF ADULT T-CELL LEUKEMIA/LYMPHOMA.

Tajima K, Tominaga S
Dept. Epidemiology, Aichi Cancer Center Res. Inst., Chikusa-ku, Nagoya 464, Japan
Gan To Kagaku Ryoho; 8(7):1009-1016 1981

In order to study adult T-cell leukemia/lymphoma (ATLL), which is prevalent in Kyushu, an etiological hypothesis of ATLL is proposed. ATLL is found in limited zones in Kyushu, mainly in rural and coastal areas, which are warm in winter and humid in summer. The geographical distribution of filariasis which accompanies several lymphoreticular ailments and was prevalent until 20 yr ago, was found to be closely correlated with that of patients with ATLL. It was also suggested from analysis of the chronological changes in the av wt and height of school children by prefecture that the nutritional condition of the inhabitants of Kyushu might have been poorer than that of other districts, especially in the past. In these respects, it is conceivable that repeated exposure to filarial infection in association with undernourishment and some other factors might have played an important role in the etiology of ATLL. (30 Refs) (In JPN)

5. LYMPHOMAS AND LEUKAEMIAS. PART 1: TROPICAL AFRICA.

Olweny CL
Uganda Cancer Inst., P.O. Box 3935, Kampala, Uganda
Clin Haematol; 10(3):873-893 1981

Burkitt's lymphoma is extensively reviewed with briefer consideration of lymphocytic and histiocytic lymphomas, and leu-

kemias in tropical Africa. Tumors of the lymphoreticular syste m, which are prominent in the area, account for 15% of all malignant diseases in Uganda. Epidemiology, etiology, clinical features and staging, pathology, differential diagnosis, treatment (surgery, chemotherapy, radiotherapy), complications, and prognosis of Burkitt's lymphoma are extensively detailed. Distinctive pathological features of Hodgkin's disease in tropical Africa include an excess of the mixed cellularity and lymphocytic depletion types and a relative deficiency of the lymphocytic predominant and nodular sclerosis types. The incidence rate of lymphocytic and histiocytic lymphoma in Uganda is slightly less than in England and Wales but the pattern in relation to age is somewhat different. The patterns of leukemias in tropical Africa, clinical features, hematological findings, and prognosis, are reviewed. (59 Refs)

EPIDEMIOLOGY AND ETIOLOGY OF NON-HUMAN LEUKEMIA AND LYMPHOMA

6. SPONTANEOUS LYMPHOMAS IN SJL/J-(V+) MICE: ECOTROPIC AND DUALTROPIC VIRUS EXPRESSION IN NORMAL AND LYMPHOMATOUS TISSUES.

De Rossi A, D'Andrea E, Colombatti A, Fischinger PJ, Chieco-Bianchi L

(c/o Chieco-Bianchi) Lab. Oncology, Inst. Pathological Anatomy, Univ. Padova, Via Gabelli 61, 35100 Padova, Italy

JNCI; 67(6):1241-1250 1981

Approx 60% of inbred SJL/J-(v+) adult mice having high levels of ecotropic endogenous XC+ virus showed virus activation within the first mo of life, while the others produced virus at comparable levels later on. In an attempt to correlate the time of virus activation with the incidence and latency of lymphomas, the tails of 57 1-and 2-mo-old mice were tested for virus presence, and the mice were then observed for lymphoma appearance. While all 2-mo-old mice expressed ecotropic virus, only 63% of the 1-mo-old mice were virus-positive. However, no relationship existed between early virus production (within 1 mo) or late virus production and lymphoma latency, total lymphoma incidence, and histopathology. In contrast with high titers of XC+ virus in tail tissues of diseased mice, a markedly low virus content was found in lymphomatous organs. This difference was not due to selective growth of poor virus-producer cells or to inhibitory factors possibly released by the inflammatory cell component. Viral protein content and XC+ virus titer were not closely correlated in the neoplastic organs. Search for XC- viruses revealed that only 1 of 6 aged normal and 16 of 19 lymphomatous mice produced viruses that grew on mink lung cells. By use of a standard limiting dilution cloning procedure, four isolates were obtained that showed tropism for both murine and heterologous cells. Three of these isolates induced cytopathic changes similar to those induced by MCF viruses on mink lung cells but not on mouse cells. Interference and neutralization assays performed to better characterize the virus envelope properties further indicated that SJL/J isolates had features typical of MCF dualtropic viruses. (Author abstract) (67 Refs)

CYTOGENETIC AND MORPHOLOGIC STUDIES

7. MONOSOMY 7 IN CHILDHOOD: A PRELEUKAEMIC STATE (MEETING ABSTRACT).

Chessells JM, Sieff CA, Pickthall HJ, Lawler SD

Departments of Haematology and Immunology, Hospital for Sick Children and Institue of Child Health, London, England

Br J Haematol; 49(1):129 1981

Between 1976 and 1979 Monosomy 7 was diagnosed in six boys aged 5 1/2 mo to 8 yr. Presenting features included hepatosplenomegaly (5/6), respiratory infections (4/6), pallor (2/6) and skin infections (1/6). Hematological features included a leukoerythroblastic anemia with leukocytosis and thrombocytopenia, and a hyperplastic marrow with a slight excess of blasts. Fetal Hb was normal or mildly raised (2/6), neutrophil function tests showed defective chemotaxis with reduced kiling, despite a normal nitroblue tetrazolium test. Cytogenic analysis of the marrow showed a preponderence of cells with Monosomy 7; the blood lymphocytes were normal. In three patients disease progressed to acute myeloid leukemia (AML) after 3 wk to 23 mo; the only patient who remitted received 6-mercaptopurine and prednisolone, but relapsed 16 mo later. A fourth child died from anemia and respiratory infection and a fifth developed massive splenomegaly and terminal myelofibrosis. The sixth patient is still in a stable state. Monosomy 7 is one of the commoner myeloproliferative states in childhood and carries a high risk of progressing to AML. The acute phase is usually resistant to chemotherapy, but even if responsive, treatment does not result in elimination of the abnormal clone. Allogeneic bone marrow transplantation should be considered in cases with a suitable donor. (no Refs)

8. CANCER CYTOGENETICS: A RE-EVALUATION OF ITS SIGNIFICANCE.

Hsu TC

Dept. Cell Biology, Univ. Texas, M. D. Anderson Hosp. and Tumor Inst., Houston, TX, 77030

Med Pediatr Oncol; 9(5):524-525 1981

Cytogenetics of familial and nonfamilial human cancers and of cancers in experimental animals are described. Specific chromosomal aberrations have been associated with human cancers including retinoblastoma, Wilm's tumor, and renal cell carcinoma. Chromosomal changes in medullary thyroid neoplasia and Gardner's syndrome have been reported. Nonrandom chromosomal alterations have been observed in murine T-cell leukemia and in neurogenic tumors induced in rats. Chromosomal aberrations have been noted in various human leukemias and lymphomas. (no Refs)

BIOCHEMICAL, IMMUNOLOGICAL AND OTHER CELL BIOLOGY STUDIES

9. ABNORMAL LYMPHOCYTES IN X-LINKED LYMPHOPROLIFERATIVE SYNDROME.

Seeley J, Sakamoto K, Ip SH, Hansen PW, Purtilo DT
Dept. Pathology, Univ. Massachusetts Medical Sch., Worcester, MA
J Immunol; 127(6):2618-2620 1981

Helper and suppressor T cells (labeled by OKT4 and OKT8 antisera, respectively,) were studied in males with X-linked lymphoproliferative syndrome (XLP), and in their mothers (carriers), asymptomatic brothers, maternally related male cousins (males at risk), and sisters (females at risk). Carrier mothers and both females and males at risk had normal mean percentages of OKT4 and OKT8 cells. However, XLP patients showed significantly lower OKT4 and higher OKT8 percentages compared with healthy controls; abnormally low OKT4:OKT8 ratios were expressed by 6/10 patients with hypogammaglobulinemia and/or lymphoma. Abnormally high OKT4:OKT8 ratios were found in several of 13 males at risk. Among the subjects at risk, OKT4:OKT8 ratios tended to be highest in those who had antibodies to Epstein-Barr virus (EBV) viral capsid antigen but not to EBV nuclear antigen. The ratios may useful in evaluating males at risk for XLP even before they become EBV-seropositive. (24 Refs)

10. CYTOLOGY OF LYMPHOMAS INVOLVING THE MULTIPLICATIVE ARM OF THE FOLLICULAR CENTER CELL SYSTEM (MEETING ABSTRACT).

Rebuck JW
Department of Pathology, Henry Ford Hospital, Detroit, MI, 48202
Am J Clin Pathol; 76(3):356 1981

Common follicular lymphomas are failures in transformation of follicular center cell (FCC) lymphocytes. But fully transformed large non-cleaved cells are migrating multipliers which account for the poor course of their diffuse lymphomas. A similar, diffuse multiplication of undifferentiated lymphocytes, one daughter-cell step below the large non-cleaved, comprise the lymphocytes of Burkitt's, non-Burkitt's, and B-immunoblastic leukemia (FAB L3). Diffuse, small cleaved cell lymphomas are three daughter-cell stages below; the rare small lymphocytic lymphoma diffuse with high mitotic activity, four stages more differentiated. Conversion of the multiplicative arm of FCC to plasma cell production results: in the plasmacytoid lymphocyte overgrowth of Waldenstrom's macroglobulinemia; in the mixture of large non-cleaved cells and plasmablasts in immunoblastic sarcoma (large cell, immunoblastic); or, if solely to plasmablasts and proplasmacytes, in myeloma. Imprint or bone marrow smear cytology will be presented for each of the above lymphomas and their variants. (no Refs)

EXPERIMENTAL STUDIES INVOLVING CHEMICAL AGENTS AND IRRADIATION

11. T-CELL LEUKEMIA INDUCED BY 1-PROPYL-1-NITROSOUREA IN FISCHER RATS.

Imamura N, Saito O, Dohy H, Ogiu T
Dept. Internal Medicine, Res. Inst. Nuclear Medicine and Biology, Hiroshima Univ., Kasumi 1-2-3, Hiroshima, Japan
Experientia; 37(12):1339-1340 1981

T-cell leukemia was induced at a high rate in female Fischer rats by continuous oral administration of 1-propyl-1-nitrosourea. No association of oncorna viruses were found in the leukemogenesis. (Author abstract) (10 Refs)

12. ETHYLENE OXIDE (ETO): EVIDENCE OF CARCINOGENICITY.

Coene RF
National Inst. for Occupational Safety and Health, Cincinnati, OH
Vet Hum Toxicol; 23(6):439-443 1981

The potential of ethylene oxide (EtO) as an occupational carcinogen is discussed. Production, use, potential for occupational exposure, evidence of carcinogenicity in experimental animals, mutagenic and reproductive effects, epidemiologic evidence of cancer in humans, exposure standards, and guides are reviewed. Results in sub-mammalian test systems (Salmonella typhimurium, Escherichia coli, Neurospora crassa, Tradescantia paludosa, and Drosophila melanogaster) have indicated mutagenic properties of EtO. EtO has caused statistically significant increases in mononuclear cell leukemia in female Fisher 344 rats. Among male Fisher 344 rats, EtO induced peritoneal mesothelioma originating in the testicular mesothelium. Investigation of possible adverse effects (analysis of chromosomal aberrations in lymphocytes for all exposed workers and sperm analysis for the men) has shown higher incidence of aberration and sister chromatid exchange among workers exposed to EtO. Cases of peripheral neuropathy among exposed workers have been reported. The present standard (1-10 ppm as 8 hr time-weighted av) may need to be reexamined; its adoption preceded recognition of the carcinogenic potential of EtO and was intended only to protect against acute and nonmalignant chronic effects. (no Refs)

EXPERIMENTAL STUDIES: DNA TUMOR VIRUSES

13. INDUCTION OF LYMPHOMAS AND TUMOR ANTIGEN BY MAREK'S DISEASE VIRUS IN TURKEYS.

Elmubarak AK, Sharma JM, Witter RL, Nazerian K, Sanger VL
U. S. Dept. Agriculture, SEA-AR, Regional Poultry Res. Lab., 3606 E. Mount Hope Road, East Lansing, MI, 48823
Avian Dis; 25(4):911-926 1981

Mycoplasma-free turkeys were inoculated with the highly pathogenic GA isolate of Marek's disease (MD) virus (MDV), and were observed for lympholytic and lymphoproliferative lesions and humoral and cellular immunocompetence. Inoculated turkey poults became persistently viremic with MDV, with levels of circulating MDV that were lower than in similarly inoculated specific-pathogen-free chickens. The early lytic phase of MD with lymphoid cell destruction and appearance of viral

antigen in lymphoid organs was less pronounced than in chickens. Gross lesions in turkey poults after MDV infection were most frequent in spleen and liver but also involved kidneys, gonad, heart, thymus, and peripheral nerves. MD tumors contained cells that reacted with antiserum prepared against chicken MD-tumor-associated surface antigen. This result indicated that MDV induced cellular transformation in turkeys and that the tumor-associated antigen in chickens and turkeys cross-reacted. Several in vitro-propagating B-cell lines were developed from tur key lymphomas. MD in turkeys resulted in immunodepression as it did in chickens. Circulating lymphocytes from turkeys that eventually died of MD or had developed gross tumors were deficient in response to Concanavalin A. (19 Refs)

EXPERIMENTAL STUDIES: RNA TUMOR VIRUSES

14. SPECIFIC INTEGRATION OF REV PROVIRUSES IN AVIAN BURSAL LYMPHOMAS.

Noori-Daloii MR, Swift RA, Kung HJ, Crittenden LB, Witter RL (c/o Kung) Dept. Biochemistry, Michigan State Univ., East Lansing, MI, 48824
Nature; 294(5841):574-576 1981

The structure of non-defective reticuloendotheliosis virus (nd Rev) proviruses in bursal lymphomas was characterized. The DNAs extracted from bursal tumors induced by the chick syncytial virus (CSV) strain of nd Rev were digested with restriction endonucleases, electrophoresed in agarose gels, and hybridized to probes specific for the nd Rev genomes and the oncogene of MC-29 virus. Linkage between REV proviruses and the c-myc gene was determined by EcoRI endonuclease digestion and confirmed by digestion with other restriction enzymes. The results suggested that in each tumor, at least one REV provirus was integrated next to the c-myc gene (on 1/2 homologous chromosomes); the latter gene was strongly implicated in lymphomagenesis. The REV proviruses in 22/25 tumors characterized were linked to c-myc. The sizes of the EcoRI linkage fragments varied from 11 to 22 kilobases (kb). The majority of viral sequences appeared to be present in the proviruses. Thus, structural alterations giving rise to the shortened 11-kb tumor-specific (TS) band probably involved the surrounding cellular sequence. The high intensity of the 11-kb TS band, along with its larger size compared to the unintegrated viral DNA, suggested that amplification of REV provirus and of its surrounding cellular sequences had occurred. Tumors 1 and 8 contained eight and one copies of the proviral sequences, respectively. Structural alteration in the REV provirus and its adjacent cellular sequences are discussed in relation to transformation. (23 Refs)

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As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

CHEMICAL CARCINOGENESIS

1. CHEMICAL CARCINOGENESIS.
Farber E
Dept. Pathology, Univ. Toronto, 100 College St., Toronto, ON M5G 1L5, Canada
N Engl J Med; 305(23):1379-1389 1981

2. N-HEXANE AND ITS TOXICOLOGIC EFFECTS. A REVIEW.
Jorgensen NK, Cohr KH
Harevaenget 44, DK-4200 Slagelse, Denmark
Scand J Work Environ Health; 7(3):157-168 1981

3. SAFROLE: ITS METABOLISM CARCINOGENICITY AND INTERACTIONS WITH CYTOCHROME P-450.
Ioannides C, Delaforge M, Parke DV
Dept. Biochemistry, Univ. Surrey, Guildford, Surrey GU2 5XH, England
Food Cosmet Toxicol; 19(5):657-666 1981

RADIATION CARCINOGENESIS

4. CARCINOGENIC, MUTAGENIC, TERATOGENIC WORKSHOP.
Sutt H, Hall E, Frei E
Dept. Radiation Medicine, Massachusetts General Hosp., Boston, MA, 02114
Cancer Clin Trials; 4(Suppl):37-41 1981

5. DOSIMETRY OF THE ATOMIC BOMB SURVIVORS.
Sinclair WK, Failla P, Bond VP, Loewe WE, Kerr GD, Auxier J, Wyckoff OH, Maruyama T, Schull JW, Land EC, Dobson LR, Mays WC, Seymour J
Argonne Natl. Lab., 9700 South Cass Ave., Argonne, IL, 60439
Radiat Res; 88(3):437-447 1981

DIETARY FACTORS IN CARCINOGENESIS

6. NUTRITION AND CANCER: A REVIEW.
Muller E, Rickenbach M
Institut fur Sozial- und Praventivmedizin, Universitat Zurich, Gloriastrasse 32 B, 8006 Zurich, Switzerland
Praxis; 70(43):1903-1912 1981
In GER

7. FLAVONOIDS, MUTAGENS, AND CITRUS.
Horowitz RM
U. S. Dept. Agriculture, Agricultural Res. Service, Fruit and Vegetable Chemistry Lab., Pasadena, CA, 91106
ACS Symp Ser; 170:43-59 1981

EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

8. ETIOLOGICAL CONCEPTS IN CERVICAL CARCINOGENESIS.
Kessler II
Dept. Epidemiology and Preventive Medicine, Univ. Maryland Sch. Medicine, 655 West Baltimore St., Baltimore, MD, 21201
Gynecol Oncol; 12(2,part2):S7-S24 1981

9. CURRENT CONCEPTS ON THE AETIOPATHOGENESIS OF ACUTE LEUKAEMIA.
Torres A, Martinez Guibelalde F, Gomez Garcia P, Garcia Castellano JM, Manzanares Escribano MR
Jefe Servicio Hematologia, Ciudad Sanitaria 'Reina Sofia' de la Seguridad Social, Cordoba, Spain
Sangre (Barc); 26(5B):700-717 1981
In SPA

10. CANCER FAMILY SYNDROME.
Svendsen LB, Bulow S
Kirurgisk-gastroenterologisk afdeling, Bispebjerg hospital, Copenhagen, Denmark
Ugeskr Laeger; 143(42):2713-2716 1981
In DAN

11. GENETIC AND BIOCHEMICAL STUDIES WITH ATAXIA TELANGIECTASIA.
Huang PC, Sheridan RB
Dept. Biochemistry, Sch. Hygiene and Public Health, Johns Hopkins Univ., Baltimore, MD, 21205
Hum Genet; 59(1):1-9 1981

ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN CARCINOGENESIS

12. THE HEALTH EFFECTS AND ECOLOGICAL SIGNIFICANCE OF CHLORINE RESIDUALS IN WATER.
Kalmaz EV, Kalmaz GD
Univ. Tennessee, Univ. Station 8163, Knoxville, TN, 37916
Chemosphere; 10(10):1163-1175 1981

13. CHEMICAL AND ENVIRONMENTAL AGENTS IN GASTROINTESTINAL CARCINOGENESIS.
Deschner EE, De Cosse JJ, Sherlock P
Lab. Digestive Tract Carcinogenesis, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Clin Gastroenterol; 10(3):755-771 1981

CELLULAR AND MOLECULAR MECHANISMS IN CARCINOGENESIS

14. THE REPAIR OF DNA DAMAGE: RECENT DEVELOPMENTS AND NEW INSIGHTS.
Friedberg EC, Bonura T, Love JD, McMillan S, Radany EH, Schultz RA
Dept. Pathology, Lab. Experimental Oncology, Stanford Univ., Stanford, CA, 94305
J Supramol Struct Cell Biochem; 16(1):91-103 1981

MODIFICATION OF CARCINOGENESIS

15. ROLE OF HORMONES INCLUDING DIETHYLSTILBESTROL (DES) IN THE PATHOGENESIS OF CERVICAL AND VAGINAL INTRAEPITHELIAL NEOPLASIA.
Robboy SJ, Truslow GY, Anton J, Richart RM
Dept. Pathology, Massachusetts General Hosp., Boston, MA, 02114
Gynecol Oncol; 12(2,part2):S98-S110 1981

16. PROSTAGLANDINS AND CANCER: A REVIEW OF TUMOR INITIATION THROUGH TUMOR METASTASIS.
Honn KV, Bockman RS, Marnett LJ
Dept. Biological Sciences, Wayne State Univ., Detroit, MI, 48202
Prostaglandins; 21(5):833-864 1981

VIRAL AND IMMUNOLOGICAL ASPECTS OF CARCINOGENESIS

17. GENITAL CANCER AND VIRUSES.
Rapp F, Jenkins FJ
Dept. Microbiology, Pennsylvania State Univ. Coll. Medicine, Hershey, PA, 17033
Gynecol Oncol; 12(2,part2):S25-S41 1981

18. VIRUS PAPILLOMAS IN HUMANS.
Nasemann T
Univ.-Hautklinik Eppendorf, Martinstr. 52, D-2000 Hamburg 20, W. Germany
Hautarzt; 32(11):601-606 1981
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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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EPIDEMIOLOGY AND ETIOLOGY OF HUMAN LYMPHORETICULAR MALIGNANCIES: VIRAL STUDIES

1. DETECTION OF THE HUMAN T CELL LYMPHOMA VIRUS P19 IN CELLS OF SOME PATIENTS WITH CUTANEOUS T CELL LYMPHOMA AND LEUKEMIA USING A MONOCLONAL ANTIBODY.

Robert-Guroff M, Ruscetti FW, Posner LE, Poiesz BJ, Gallo RC
Lab. Tumor Cell Biology, NCI, NIH, Bethesda, MD, 20205
J Exp Med; 154(6):1957-1964 1981

The p19 monoclonal antibody for human T cell lymphoma virus (HTLV) and expressio n of HTLV p19 in cells of patients with leukemia and lymphoma are described. Radioimmune precipitation assay for HTLV proteins demonstrated the specificity of the antibody. Among the iodinated HTLV proteins, only p19 could be specifically precipitated. In indirect immune fluorescence assays, anti-p19 specifically labeled only HTLV-producing cells. Transformed HUT78 cells, derived from a patient with either cutaneous T cell lymphoma or leukemia (CTLC), did not produce HTLV and were negative for p19. Both HUT102 parental cells and clones were 60-70% positive, suggesting that viral expression might be related to cell cycling. CTCL-2 and CTCL-3 cells were 5% and 12% positive, respectively. The fluorescent labeling of virus-positive cells was restricted to the cell membrane. Only fixed cells were labeled, supporting the idea that p19 is an internal HTLV protein and not an envelope component. HTLV p19 is not expressed in most malignant T cells, indicating that replicating HTLV is not present. The monoclonal antibody to HTLV p19 provides an assay of HTLV expression for determining the frequency of HTLV replication in human T cells and for studying the regulation of viral gene expression. (14 Refs)

2. DETECTION BY RADIOIMMUNOASSAY OF ANTIGENS RELATED TO THE P30 POLYPEPTIDES OF PRIMATE TYPE C ONCOVIRUSES IN PERIPHERAL LEUKOCYTES FROM PATIENTS WITH CHRONIC MYELOGENOUS LEUKAEMIA.

Toth FD, Vaczi L, Kiss J, Rethy A, Kiss A, Rak K
Inst. Microbiology, Univ. Medical Sch., 4012 Debrecen, Hungary
Acta Virol (Praha); 25(6):376-380 1981

Leukocytes from patients with chronic myelogenous leukemia were examined for antigens related to the p30 polypeptides of baboon endogenous virus (BaEV) and gibbon ape leukemia virus (GaLV). Samples from patients with the quiescent phase of the disease proved to be negative or contained p30 of BaEV as the only viral antigen. In cases of blastoid crisis or acceleration, an antigen related to p30 of GaLV could be detected. In five of six patients, acceleration or blastoid crisis was preceded by expression of GaLV p30. (Author abstract) (15 Refs)

3. REVERSE TRANSCRIPTASE IN THE BLOOD OF CHILDREN WITH ACUTE LEUKAEMIA (MEETING ABSTRACT).

Kiss S, Schuler D
2nd Department of Pediatrics, Semmelweis University Medical School, Budapest, Hungary
Ninth Congress of the Haematological Society, October 1-3, 1981, Debrecen, Hungary. The Society 175 pp., 1981.

The problem of viral origin of acute leukemia in childhood was studied. As it is well known, several animal leukemias are of viral origin. These viruses are characterized by a virus-specific enzyme, reverse transcriptase, the detection of which in different tissues support vital organs. An exact method for the detection of the enzyme from leukemic tissues was elaborated. Using the method, the following conclusions were made. 1) 1-2 mg of Rauscher leukemic murine spleen is enough for the exact determination of viral infection. 2) The specificity of the enzyme reaction was verified. With the help of the enzyme reaction blood samples of acute leukemic children examined and the results are now reported. (no Refs)

EPIDEMIOLOGY AND ETIOLOGY OF HUMAN LYMPHORETICULAR MALIGNANCIES: OTHER STUDIES

4. FAMILIAL HAIRY CELL LEUKAEMIA (MEETING ABSTRACT).

Rundles RW, Huang AT
Department of Medicine, Duke University Medical Center, Durham, NC
Sixth Meeting of the International Society of Haematology, European and African Division, August 30-September 4, 1981, Athens, Greece. Hellenic Society of Haematology 409 pp., 1981.

We studied 2 families with hairy cell leukemia (HCL) occurring in several 1st degree relatives. In one family, splenectomy in a woman at age 30 led to the diagnosis of 'reticuloendotheliosis'. At age 51 she was still well but had abnormal lymphocytes in her blood. Her brother at age 45 developed HCL with progressive splenomegaly and pancytopenia. Splenectomy was beneficial, but after 14 mo his disease progressed and he died of pneumococcal meningitis. Two healthy young adults in the second generation had a small percentage of abnormal lymphocytes in their blood. In the second family, HCL occurred in a man aged 74, his son, 46 and a grandson, 24. The older two had large spleens and pancytopenia. Their blood and marrow contained large numbers of characteristic hairy lymphocytes evident in stained blood films, and by phase and electron microscopy. The abnormal lymphocytes had dual surface markers for B (SIg+) and T cells (T-antigen+) and were both Ia+. Sixty percent of abnormal lymphocytes in the older man were TRAP (tartrate-resistant acid phosphatase) positive. His son's abnormal lymphocytes were TRAP negative when first studied but later 30% of them became weakly positive. The grandson was well but 80% of his blood lymphocytes had HCL morphology similar to that of the lymphocytes of his father and grandfather. The abnormal cells were TRAP negative at present. (no Refs)

5. HAIRY CELL LEUKEMIA IN THREE SIBLINGS: AN APPARENT HLA-LINKED DISEASE.

Wylin RF, Greene MH, Palutke M, Khilanani P, Tabaczka P, Swiderski G
Harper Hosp., 3990 John R. St., Detroit, MI, 48201
Cancer; 49(3):538-542 1982

In a sibship of 11 adults the HLA haplotype A1, B7 occurred in four brothers, three of whom developed hairy cell leukemia (HCL) within a 7-year period. While this haplotype does not appear to occur with increased frequency in random cases of HCL, the fact that three cases of this uncommon and unique disorder occurred within one family and affected siblings with a common haplotype strongly suggests a genetic linkage. (Author abstract) (21 Refs)

6. NON-HODGKIN'S LYMPHOMA OCCURRING IN TWINS (MEETING ABSTRACT).

Istvan M, Marton E, Istvan L, Rohonyi B

Institute of Pathology, University Medical School, Pecs, Hungary

Ninth Congress of the Haematological Society, October 1-3, 1981, Debrecen, Hungary. The Society 175 pp., 1981.

The etiology and pathogenesis of malignant lymphomas is controversial. The possible etiology, as Epstein-Barr virus in Burkitt's lymphoma, could only emerge in the case of some malignant lymphomas. The etiologic factors of malignant lymphomas, which occur frequently in immunodeficiency during immunosuppressive treatment and autoimmune disorders, are mostly unknown. The familial occurrence of malignant lymphomas is rare. Different types of non-Hodgkin's lymphomas observed in the case of twins are discussed by the authors. At the age of 17 in the first member of the twins - contrary to the experience that low malignant lymphoma does not occur under the age of 20-immunocytoma was observed; survival was for 36 months. At the age of 22 acute lymphoblastic leukemia of T cell origin developed in his twin brother, survival was 7 months. The possible etiologic factors are analyzed by familial and anamnestic investigations. (no Refs)

7. CHARACTERIZATION OF THE LYMPHOID POPULATION IN THE LEUKAEMIA-LIKE REACTION OF AN INFANT WITH DOWN'S SYNDROME (MEETING ABSTRACT).

Miale TD, Nasrallah AG, Colquitt K, Elliott AS, Kukolich MK, Friedman S

Cook Children's Hospital, Fort Worth, TX, 76102

Sixth Meeting of the International Society of Haematology, European and African Division, August 30-September 4, 1981, Athens, Greece. Hellenic Society of Haematology 409 pp., 1981.

Newborn infants with Down's syndrome frequently present with a circulating lymphocyte population which, morphologically, is almost indistinguishable from acute lymphoblastic leukemia (ALL). This is usually designated 'leukemia-like reaction in Down's syndrome' (LLR-DS). In contrast with ALL, however, the usual natural history of LLR-DS is spontaneous remission. We attempted to characterize LLR-DS immunologically in comparison with childhood ALL. Natural killer (NK) cells were somewhat reduced in comparison with pediatric and adult controls but not in relationship to another patient with Down's syndrome without LLR-DS. (no Refs)

8. CEREBRAL DEGENERATION IN DOWN'S SYNDROME.

Gath A

Dept. Child Psychology, West Suffolk Hosp., Hardwick Lane, Bury St. Edmunds, Suffolk P33 2QZ, England

Dev Med Child Neurol; 23(6):814-817 1981

Physical and mental deterioration in patients with Down's syndrome (DS) is reviewed. Although an absolute limit to the mental age attainable by children with DS is apparent, no conclusive evidence indicates deterioration of mental function in childhood. In contrast, adults with DS show increased mortality and deterioration similar to those in Alzheimer's disease. Studies of DS patients an d their families show increased rates of congenital malformations, Hodgkin's disease, lymphocytic leukemia, and lymphosarcoma, suggesting a common genetic component for these conditions. (17 Refs)

9. BURKITT TYPE LYMPHOMA IN CAUCASIAN CHILDREN (MEETING ABSTRACT).

Philip T, Lenoir GM, Bryon PA, Gerard-Marchant R, Souillet G, Philippe N, Freycon F, Brunat-Metingyn M

Centre Leon-Berard, 28 rue Laennec, 69373 Lyon, France

UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

A retrospective analysis of 87 cases of Caucasian childhood non-Hodgkin malignant lymphoma (NHL) from Lyon, France, was performed. All the cases were diffuse lymphomas, but 47 were diagnosed as monomorphic B small non-cleaved NHL, pathologically undistinguishable from Burkitt's lymphoma (BL). BL could then be the most frequent childhood lymphoma in France. This homogeneous series allows better definition of the characteristics of BL within NHL. Age distribution is similar to that of endemic BL, with a sex ratio of 3.7/1. Abdominal masses are initially present in 68% of the cases, whereas jaw is involved in only 4%. The disease is characterized by its overwhelming evolution in the absence of therapy. However, complete remission (CR) is usually obtained, following the first chemotherapy regimen. Most relapses are observed between 3 and 8 mo. Death could be related to CNS, local recurrence or bone marrow involvement. Ninety % of the patients alive with no evidence of disease 8 mo after CR can be considered as definitely cured. Less than 20% of these cases are associated with Epstein Barr virus (EBV). In all cases studied so far, cytogenetical rearrangements of chromosome 8 considered as characteristic of BL, (t(8;14) or t(8;22)) have been found. Our study on Caucasian children with NHL indicates that from histological, clinical and cytogenetic criteria, nearly half the cases are very similar to African BL. Even if EBV was rarely found to be associated with our cases, the eponym of BL could correspond to a world wide lymphoma. (no Refs)

10. BURKITT'S LYMPHOMA.

Ambrus JL, Ambrus CM

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J Med; 12(6):385-413 1981

Clinical and epidemiologic features of Burkitt's lymphoma are reviewed. Epidemiologic studies suggest that simultaneous infection with Epstein-Barr (E-B) virus and malaria may be involved as etiologic agents. On the other hand we have found that in the Amazon region of Brazil and Peru both malaria and E-B virus infection is common among children, yet Burkitt's lymphoma is rare. The possibility exists that other concomitant etiologic agents and genetic factors are also involved. Several investigators suggested the possible involvement of Reo 3 virus. We have found antibodies against Yaba virus. A labor atory worker who accidentally inoculated himself with Yaba virus developed a histiocytoma which when inoculated into Asiatic monkeys produced typical Yaba tumors. This was the first case that Koch's postulates were fulfilled in a virus induced neoplasm in man. Therapeutically, the best clinical results were obtained in those patients who were treated with small doses of cyclophosphamide. On the basis of somewhat inadequate follow-up studies, it is estimated that '5 year cures' were obtained in about 10% of the patients. (Author abstract) (44 Refs)

11. TRANSFORMATION OF WALDENSTROM'S MACROGLOBULINEMIA IN A HIGH GRADE MALIGNANT LYMPHOMA OF IMMUNOBLASTIC TYPE (MEETING ABSTRACT).

Wust I, Emmerich B, Pemal M, Lechner S, Rastetter J
Department of Haematology and Oncology, Technical University Munich, Munich, W. Germany
Sixth Meeting of the International Society of Haematology, European and African Division, August 30-September 4, 1981, Athens, Greece. Hellenic Society of Haematology 409 pp., 1981.

Transformation of a chronic hemopoetic proliferative disorder in a morphologic different acute high grade malignancy is a common event in chronic granulocytic leukemia and occurs in low incidence in some Non-Hodgkin lymphomas, but is unusual for Waldenstrom's macroglobulinemia. Clinical data will be reported from a 67 yr old male patient in whom diagnosis of macroglobulinemia was made by monoclonal IgM, enlargement of spleen, liver and abdominal lymph nodes and bone marrow aspiration and biopsy. He was treated with steroids and cyclophosphamide for three mo. Then an acute acceleration of lymph node and organ infiltration with severe hemolytic anemia developed. The monoclonal IgM was further present, and now also kappa 1-chains were excreted in the urine. Bone marrow biopsy and post mortem examination revealed a disseminated high grade malignant lymphoma from immunoblastic type. The permanent production of the same M gradient suggests that both malignancies derived from one B-cell clone. (no Refs)

12. MOLECULAR STUDIES ON ACQUIRED ALPHA THALASSAEMIA ASSOCIATED WITH PRELEUKAEMIA (MEETING ABSTRACT).

Anagnou N, Chesbro B, Colbert D, Wright G, Nienhuis A, Deisseroth A
National Institutes of Health, Bethesda, MD, 20205
Sixth Meeting of the International Society of Haematology, European and African Division, August 30-September 4, 1981, Athens, Greece. Hellenic Society of Haematology 409 pp., 1981.

An acquired form of alpha thalassemia has been reported in 11 patients most of whom were of northern European origin and who presented with a dimorphic pattern in the peripheral blood, Hb H levels which range from 3-30%, and a bone marrow which shows erythroid hyperplasia with ineffective erythropoiesis, ringed sideroblasts and elevated levels of myeoloblasts. We have studied a 75 yr old wh ite man from the USA who presented with preleukemia and Hb H disease. His peripheral blood and bone marrow were as described above and Hb H levels were 25-30%. Globin chian synthetic studies in peripheral blood and bone marrow showed an alpha/beta ratio of less than 0.08. Similar results were seen by translating the poly(A+) messenger (m)RNA in a cell-free system. Northern hybridization analysis showed an alpha/beta globin mRNA ratio of less than 0.10. We have studied the arrangement of the alpha-globin gene cluster of this patient, by restriction endonuclease and Southern transfer studies of DNA isolated from his bone marrow. These studies did not reveal any major deletions in the alpha globin gene region but extensive studies with double digests are underway in both the alpha and zeta region in order to rule out small deletions involving only a few nucleotides. Our studies have shown that the acquired defect of alpha globin gene expression which has arisen during the prodrome of leukemia is not associated with large scale deletions of the alpha globin gene locus, and is due to a defect either at the transcriptional or intranuclear processing level. The studies of these patients ongoing in our laboratory as well as in those of others may provide a clear understanding of the genetic origin of the these acquired thalassemic defects and their possible relation to the leukemic syndromes of which they are a part. (no Refs)

13. DYSMYELOPOIESIS AND PRELEUKAEMIA PRODUCING FINDINGS OF 6-THALASSEMIA (MEETING ABSTRACT).

Loutradi-Anagnostou A, Loukopoulos D, Fessas P
1st Department of Medicine, University of Athens School of Medicine, Athens, Greece
Sixth Meeting of the International Society of Haematology, European and African Division, August 30-September 4, 1981, Athens, Greece. Hellenic Society of Haematology 409 pp., 1981.

Marked red cell abnormalities are not uncommon in cases of refractory anemia associated with the presence of rare blast cells in the peripheral blood. This group of diseases referred to in the literature under various names is frequently known to progress to acute myeloblastic leukemia (AML). Various enzymatic or antigenic alterations of the abnormal red cell population have been reported in the past; the present paper summarizes our observations on six patients with refractory anemia and marked red cell abnormalities suggesting beta-thalassemia for which a more detailed investigation was carried out. To-date four of these patients have already developed AML, while the rest are expected to do so eventually, as indicated by a gradual increase of blastic cells in the bone marrow. Red cell indices were low normal in all of the above cases, while red cell precursors in the marrow displayed no characteristic abnormalities. Serum iron was high normal; in no instance were any ringed sideroblasts detected. Hemoglobin studies revealed an e xtremely low HbA2 level; in one patient the gradual decrease of HbA2 was followed up over the yr during its transition to AML. HbF remained within normality in all cases. Hemoglobin biosynthesis revealed low beta/alpha ratios in all studied cases (0.28, 0.51, 0.55, 0.51 and 0.71). There was no thalassemia in any other member of the families of the patients. The low beta/alpha ratios in these cases contrast markedly with another group of refractory anemias (sideroblastic) also known to progress into AML, which display beta/alpha ratios compatible with alpha-thalassemia on biosynthesis or even manifest an acquired Hb H syndrome. It is noteworthy that the level of HbA2 is lower than half of normal in almost all cases suggesting that malfunction of one delta-gene only may not be the cause of the disturbance. (no Refs)

14. CARCINOMA OF THE LARGE BOWEL AND BLOOM'S SYNDROME.

Lerman T, Zlotogora J, Mugia M, Freund U
Dept. Human Genetics, Hadassah-Univ. Hosp., Jerusalem, Israel
Harefuah; 101(5/6):119-120,142 1981

Bloom's syndrome (BS) and adenocarcinoma of the colon were discovered in a 28-yr-old Ashkenazic woman. The etiology and clinical characteristics of BS are discussed. Predisposition to malignancy, particularly leukemia and lymphoma, in patients with BS is considered. The high frequency of BS in Ashkenazic Jews and their resultant high probability of developing cancer are discussed. (5 Refs) (In HEB)

15. BENZENE LEUKEMIA (MEETING ABSTRACT).

Braier L

Sackler School of Medicine, Tel-Aviv University, Tel-Aviv, Israel

Sixth Meeting of the International Society of Haematology, European and African Division, August 30 September 4, 1981, Athens, Greece. Hellenic Society of Haematology 409 pp., 1981.

Benzene (C6H(6)) is the only industrial chemical possessing aplastic antileukemic and leukemogenic properties in man. Toluene has no myelotoxic action in animals or in man. Other myelodepressive drugs, ie alkylating chemicals are also potentially leukemogenic in man. Acute myeloid leukemia (AML) and erythroleukemia represent the more typical examples of benzene leukemia. They show some features in common: (a) development after many yr of exposure and, in some cases, many mo after the last contact with benzene vapors; (b) leukopenia or only moderate degree of leukocytosis; (c) splenohepatomegaly discrete or absent and (d) unresponsiveness to treatment. A number of cases reported as aplastic anemia in the past might have been examples of acute leukemia with cryptoleukemia features. Hypo-aplastic anemia is frequently found among the antecedents of benzene induced leukemia. The relevance of benzene as an etiological agent for human leukemia (and lymphoma) can be clarified by carrying out a wide prospective survey on all the cases diagnosed in adults, including (a) a careful anamnesis regarding benzene exposure and (b) determination of benzene in blood and/or bone marrow specimens by gas chromatography techniques. A treatment based on the oral administration of large doses of 'antibenzene' compounds, including (1) methyl-donors much as choline, betaine and methionine; (2) thiol-aminoacids such as cysteine-HCl and l-methionine is proposed here for the treatment of all kinds of benzene hemopathy and the prevention of benzene leukemia in so-called 'preleukemic states' resulting from chronic benzene exposure. Prevention of benzene hemopathy can be achieved by (1) prohibiting the manufacture and use of consumer products (ie solvents, cleaning, 'benzines' and adhesives) containing 1% or more pure benzene; (2) lowering the concentration of benzene at the workplace air to 5 ppm or less and (3) avoiding as possible the use of benzene as a reagent for research and teaching purposes. (no Refs)

16. CANCER RISKS IN PEDIATRIC NUCLEAR MEDICINE (MEETING ABSTRACT).

Swanson MA, Hines HH

University of California Davis Medical Center, Sacramento, CA

Clin Nucl Med; 6(9S):448 1981

Because of pediatricians' interest in long term effects of radiation in childhood, the authors have prepared cancer risk estimates for three more commonly ordered pediatric scans and compared them with the spontaneous incidence of the same cancers in the unexposed population. Calculations were based on age, weight and scan dose, assuming an average life expectancy of 70 years. The BEIR III linear-quadratic model was used to estimate 30 year leukemia and bone cancer risk and the BEIR III linear model for the lifetime risk of hepatic neoplasms. Absorbed dose estimates were taken from the literature for cancer risk calculations. (no Refs)

17. ACUTE MYELOID LEUKAEMIA AND ACUTE MYELOMONOCYTIC LEUKAEMIA CONSIDERED AS SECOND MALIGNANCY (MEETING ABSTRACT).

Takacs E, Lajos I, Stefanics K, Wallacher L, Balazs M

University Medical School, Pecs, Hungary

Ninth Congress of the Haematological Society, October 1-3, 1981, Debrecen, Hungary. The Society 175 pp., 1981.

After the introduction of irradiation and cytostatic treatment of malignant tumors, especially the Hodgkin's disease and multiple myeloma, a great number of articles have been published reporting the development of the second malignancy, being independent of the first. The cases of acute myeloid and myelomonocytic leukemia, having developed after two generalized non-Hodgkin's malignant lymphomas of follicular origin, as well as carcinoma of breast and uterine are discussed. The myeloid origin of atypical cells of the bone marrow and peripheral blood can be confirmed by cytochemical, cytomorphological, and by electronmicroscopical findings. (no Refs)

18. SACCHARINE, LEUKAEMIA AND HODGKIN'S DISEASE (MEETING ABSTRACT).

Aksoy M

No affiliation given

Sixth Meeting of the International Society of Haematology, European and African Division, August 30-September 4, 1981, Athens, Greece. Hellenic Society of Haematology 409 pp., 1981.

Saccharin acts as bladder co-carcinogen when fed to rats receiving intraurethral doses of N-methyl-nitrosourea. But some were not able to confirm this. We report here 2 typical cases of leukemia and 1 with Hodgkin's disease (HD) following the use of saccharin. Case 1, 54 yr-old gynecolog used 8-10 tablets of saccharin, daily , 3 mo, to lose wt. Chronic myelogenous leukemia (CML) associated with Philadelphia chromosome and low WBC alkaline phosphotase developed. Following adequate Myleran treatment WBC count returned to normal level. After 4 yr remission, diabetes mellitus developed and following reuse of saccharin, 3 days only CML relapsed. He noticed also when he ate sweets containing non-caloric sweeters, the effect of Myleran on WBC count decreased considerably. The patient is still under treatment. Case 2, 53 yr-old man was diabetic since 16 yr. He used 10-15 tablets of saccharin daily for 15 yr. Acute myelomonocytic leukemia developed. Case 3, a 30 yr-old house-wife used approx 5-6 tablets of saccharin for 11 yrs in order to lose wt. Two yr ago the signs of HD nodular sclerosing type, stage III, appeared. Although these case reports do not prove a causal relationship between the use of saccharin and some hematologic malignancies, the findings of this association suggest that saccharin not only cause bladder carcinoma but also is involved in some types of hematologic malignancies as leukemia and HD, at least in the individuals with genetic predisposition for these malignant disorders. (no Refs)

EPIDEMIOLOGY AND ETIOLOGY OF NON-HUMAN LEUKEMIA AND LYMPHOMA

19. EPIDEMIOLOGICAL FEATURES OF FELINE MAMMARY CARCINOMA.

Hayes HM, Milne KL, Mandell CP
Environmental Epidemiology Branch, NCI, NIH, Bethesda, MD
Vet Rec; 108(22):476-479 1981

Epidemiological features of cats with mammary carcinoma were studied. In a group of 132 cats with one or more mammary tumors, 113 had carcinomas of various types (including two males). Adenocarcinoma was the predominant cell type. Thirty females with mammary carcinoma had metastases, primarily in the lung (13) or lymphatic system (9). Five cats with carcinoma had a prior or concomitant history of viral infection: feline leukemia (2), viral rhinotracheitis (2), or viral pneumonitis (1). Relative risk (RR) analysis showed significantly less risk for spayed females (RR = 0.6) than intact females (RR = 1), however both groups showed increasing risk with advancing age. The Siamese breed had a significantly higher risk (RR = 2.0) than all other female cats combined (RR = 1) and did not show significantly increasing risk after 7-9 yr of age. Unlike humans and dogs, mammary tumors in the cat are not strongly associated with ovarian tumors. Estrogen receptors were not found in 90% of cat breast tumors, suggesting a particular suitability for evaluating therapeutic regimens for non-estrogen dependent breast cancers. (28 Refs)

CYTOGENETIC AND MORPHOLOGIC STUDIES

20. COMPARISON OF KARYOTYPE, MORPHOLOGY, ETHNIC GROUP, AGE AND SURVIVAL IN ACUTE NON-LYMPHOCYTIC LEUKAEMIA (ANLL) (MEETING ABSTRACT).

Bernstein R, MacDougall LG, Mendelow B
Departments of Human Genetics and Haematology, School of Pathology, South African Institute for Medical Research and University of the, Witwatersrand Johannesburg, South Africa
Sixth Meeting of the International Society of Haematology, European and African Division, August 30-September 4, 1981, Athens, Greece. Hellenic Society of Haematology 409 pp., 1981.

Data on 60 patients with ANLL were analyzed to assess whether chromosomal pattern correlated with leukemic cell morphology, ethnic group, age, sex and survival. A significant ethnic age difference was observed; 11 of 22 black patients versus 2 of 38 white patients were children. Males predominated among the children. A higher frequency of chromosome abnormalities was detected in children yet they survived significantly longer than adults. A specific association between the t(8;21) karyotype and M2-ANLL was observed. The more differentiated morphology of M2-ANLL was associated with a significantly longer survival irrespective of karyotype, ethnic group or age. The specificity of a t(15;17) karyotype in M3-ANLL was confirmed. Monosomy 7 was non-randomly found in 2 children with a preleukemic phase. Patients with a normal karyotype tended to survive longer than those with abnormal karyotypes, but this difference was only of borderline significance in adults and not significant when assessed in adults and children. The patient's age and capacity of the leukemic cell to differentiate appear to be more important than ethnic group or karyotype in determining survival. Non-random chromosome aberrations in ANLL appear to be worldwide and are unrelated to ethnic differences between South African blacks and whites. (no Refs)

21. MEMBRANE MARKERS, TDT AND ULTRASTRUCTURAL CYTOCHEMISTRY IN APPARENTLY NON MYELOID LEUKEMIAS (MEETING ABSTRACT).

Zittoun R, Marie JP, Perrot JY, Zittoun J, Boucheix C, Rosenfeld C
Service d'Hematologie de l'Hotel Dieu Paris, Paris, France
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

A prospective study including the determination of the common acute lymphoblastic antigen (CALLA), the human T lymphocyte antigen (HUTLA), the terminal deoxynucleotidyl transferase (TdT) and the ultrastructural detection of peroxidase activity (POEM) was performed on 16 apparently non myeloid, non T non B acute leukemias. These patients were selected from 73 adult leukemic patients by the n egativity of their routine cytochemical myeloid markers (myeloperoxidase, Sudan Black B, chloracetate activity), and the absence of B (surface IG) or T (spontaneous sheep (SRBC rosettes) markers. The anti CALLA serum was prepared by rabbit's immunization against Reh cell line. The TdT assay was measured using the biochemical method of Bollum modified by Hoffbrand et al. The detection of POEM was performed according to the techniques of Breton-Gorius et al. After this multiparametric study, all leukemias could be classified as following: 6 CALL (CALLA+), 1 pre-T ALL (CALLA+, HUTLA+), 2 poorly differentiated ALL (CALLA-, POEM-, TdT+), 5 poorly differentiated AML (CALLA-, POEM+), and 2 mixed leukemias (CALLA+, POEM+). The cytogenetic studies has shown that 2 of the CALL, 3 of the AML and the two mixed leukemias were Ph 1+. We conclude that POEM detection is useful to classify the apparently non myeloid leukemias with negative immunological markers. (no Refs)

22. CYTOLOGIC CHARACTERIZATION AND SIGNIFICANCE OF NORMAL KARYOTYPES IN T(8;21) ACUTE MYELOBLASTIC LEUKEMIA.

Berger R, Bernheim A, Daniel MT, Valensi F, Sigaux F, Flandrin G
Laboratoire de Cytogenetique, Centre Hayem, Hopital Saint-Louis, 2 Place du Dr. Fournier, 75475 Paris Cedex 10, France
Blood; 59(1):171-178 1982

A cytologic and cytogenetic study of 10 cases of acute myeloblastic leukemia with maturation and t(8;21) translocation is reported. Despite a certain polymorphic appearance, the characteristic cytologic picture, consisting essentially of large myeloblasts with an abundant cytoplasm containing a large Auer rod, allowed the presence of the chromosome anomaly to be predicted. t(8;21) translocation was attended by the loss of a sex chromosome in 7 of 10 cases. The comparative study of mitoses using cytologic and cytogenetic techniques showed that cells exhibiting normal karyotypes were essentially erythroblasts. This finding suggests that the chromosome anomaly does not affect all the bone marrow cell lines. After short-term culture, the percentage of normal karyotype mitoses diminished, as did the number of mitoses in erythroblasts. (Author abstract) (23 Refs)

23. CYTOGENETIC STUDIES IN ADULT ACUTE LEUKEMIAS.

Takeuchi J, Ohshima T, Amaki I
Dept. Genetics and Endocrinology, Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
Cancer Genet Cytogenet; 4(4):293-302 1981

Thirty-six patients with acute leukemia (31 with AML, 5 with ALL) were classified by FAB criteria, and their bone marrow cells were analyzed cytogenetically with G-banding. Chromosomal abnormalities were found in 16 patients (44%). The most common abnormality was an 8;21 translocation, accounting for 19.4% of all AML patients, that was restricted to patients with M2. In 29 treated AML patients, those with an 8;21 translocation [t(8;21) patients] showed a higher complete remission rate (83%) a nd a longer median survival (10.7 mo) than did other patients with AML; patients with only abnormal metaphases (AA patients) had the lowest complete remission rate (33%) and shortest median survival (2.7 mo). There was no difference in the remission rate and the survival between patients with only normal metaphases (N patients) and patients with abnormal metaphases (A patients). Three out of five patients with ALL had karyotypic abnormalities; the Philadelphia (Ph1) chromosome was found in one case. (Author abstract) (31 Refs)

24. THE 5Q ANOMALY (MEETING ABSTRACT).

Van den Berghe H
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Sixth Meeting of the International Society of Haematology, European and African Division, August 30-September 4, 1981, Athens, Greece. Hellenic Society of Haematology 409 pp., 1981.

Data obtained on more than 100 cases of hematologic malignancy with interstitial deletion of the chromosome 5 long arm showed that this particular chromosome anomaly may characterize a pluripotent stemcell disorder, which may express itself as (1) a refractory anemia, with or without excess of blasts, (2) a smoldering leukemia, (3) acute myelogenous leukemia and (4) acute lymphoblastic leukemia. Moreover, the 5 q- anomaly characterizes a group of secondary acute myeloblastic leukemias arising in patients treated with ionizing radiation and or alkylating agents. (no Refs)

25. SPECIFICITY OF SOME HAEMATOLOGICAL AND MORPHOLOGICAL FEATURES FOR 5Q-CHROMOSOME IN PRELEUKAEMIC PATIENTS (MEETING ABSTRACT).

Teerenhovi L, Borgstrom GH, Lintula R, Elonen E, Knuutila S, Vuopio P
3rd Department of Medicine, University of Helsinki, Helsinki, Finland
Sixth Meeting of the International Society of Haematology, European and African Division, August 30-September 4, 1981, Athens, Greece. Hellenic Society of Haematology 409 pp., 1981.

Patients with a deletion of long arm of chromosome 5 (5q-) as a sole karyotypic aberration have refractory anemia and a relatively good prognosis. Some patients are, however, known to progress to acute leukemia. The 5q-aberration is associated with a specific syndrome. Five features are usually present: macrocytic anemia, normal or low count of erythroid precursors in the bone marrow, absence of ring sideroblasts, normal or high platelet count and megakaryocytic hypolobulation. We studied 80 preleukemic patients (41 with normal and 39 with abnormal karyotype) for the presence of these 5 features. In altogether 8 patients 4 or all of the features were found. Six of them had a sole 5q- aberration, 1 a karyotype with 46, XX,5q-,22q- and 1 a normal karyotype. Among the 72 patients with less than 4 features there was only 1 patient with a sole acquired 5q- aberration; this patient had also a constitutional trisomy X. None of the featur es was in itself pathognomonic for 5q- chromosome. The most noticeable of the features, megakaryocytic hypolobulation, was also found in some patients with monosomy 7, trisomy 8, i(17q) and normal karyotype. It was always present in our patients with 5q- aberration only. We conclude that megakaryocytic hypolobulation substantiated with 3 or 4 of the other above mentioned features can be successfully used as diagnostic criteria to differentiate the patients with 5q- syndrome from other preleukaemic patients. (no Refs)

26. ANALYSIS OF THE ANDROGEN RESPONSE OF 23 PATIENTS WITH AGNOGENIC MYELOID METAPLASIA: THE VALUE OF CHROMOSOMAL STUDIES IN PREDICTING RESPONSE AND SURVIVAL.

Besa EC, Nowell PC, Geller NL, Gardner FH
Medical Coll. Pennsylvania, 3300 Henry Ave., Philadelphia, PA, 19129
Cancer; 49(2):308-313 1982

The responses of 23 patients with agnogenic myeloid metaplasia (AMM) to androgen therapy were studied. Various clinical and laboratory parameters were analyzed for their value in determining response to therapy and length of survival. Fifty-seven percent of patients responded, as determined by a sustained increase in hematocrit within 3 mo of therapy which thus eliminated the need for transfusions. Chromosome study of the abnormal hemic population was the best predictor of response: 92% of patients with normal chromosomes responded, while 78% of patients with chromosomal abnormalities did not. Responders had a mean survival time of 5 1/2 yr from the time of diagnosis as compared with 2 yr for the nonresponders. The degree of thrombocytopenia, suppression of the ferrokinetic, and lack of activity in axial skeleton on bone marrow scans indicated severly compromised hemopoiesis in the nonresponders. The results suggest that in some patients with AMM, more extensive cytogenetic alterations in the abnormal hematopoietic cells result in an inability to respond to androgen therapy and that the chromosome study is the test most accurate for predicting the outcome of therapy. (Author abstract) (29 Refs)

27. CYTOGENETIC STUDIES IN ERYTHROLEUKEMIA (M6) (MEETING ABSTRACT).

Ohyashiki K, Oshimura M
Department of Internal Medicine, Tokyo Medical College, Tokyo, Japan
Proceedings of the Japanese Cancer Association 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

Evaluation of the exact incidence of karyotypic changes and uncovering karyotypic pictures in erythroleukemia (EL) have been made difficult by the inclusion of such cases in the general category of acute nonlymphocytic leukemia (ANLL), without differentiation being made between acute myelocytic leukemia (AML) and EL. Cytogenetic studies with chromosomal banding techniques were made in twelve cases of EL (M6 in the FAB classification), to clarify whether or not any specific chromosome anomalies wer e present in EL. Of the twelve cases, four were karyotypically normal, one was partially monosomic for 7q (7q-), one was monosomic for chromosome 7, one was trisomic for chromosome 8, and the remaining five showed complex karyotypes with karyotypic instability. The detailed analyses in the five cases with complex karyotypes revealed that three of them contained the 7q- anomaly as a 'prototypic karyotype.' Since the 7q-, a monosomy 7 and a trisomy

8 have being frequently observed in AML, the present findings may suggest that there is no specific chromosome anomaly which characterizes EL, and support a notion that EL is merely a variant form of AML. In addition, possible meanings of the karyotypic instability in EL will be discussed. (no Refs)

28. TRANSLOCATION (15;17) AND ACUTE PROMYELOCYTIC LEUKAEMIA IN ITALY (MEETING ABSTRACT).

Bernasconi P, Casalone R, Pasquali F
Istituto Biologia Generale e Genetica Medica, Universita di Pavia, Pavia, Italy
Sixth Meeting of the International Society of Haematology, European and African Division, August 30-September 4, 1981, Athens, Greece. Hellenic Society of Haematology 409 pp., 1981.

Translocation between chromosomes 15 and 17 was found in 41% of a group of 80 patients with acute promyelocytic leukemia (APL) at the Second International Workshop on Chromosomes in Leukaemia. The Workshop data suggested an apparent uneven geographical distribution of the translocation, and it was pointed out that in the sample there were no Italian patients with the translocation. We report the results of the analysis of 9 Italian patients with APL. Two of them had the standard translocation (15;17) (q24;q21) and one had a cell line with a 17q- deletion. Two of the patients had other chromosome abnormalities while four had a normal karyotype. (1 Ref)

29. FEATURES OF CHROMOSOMAL ABNORMALITIES IN ATYPICAL LEUKEMIA.

Tagawa M, Tomonaga Y
Dept. Hematology, Atomic Disease Inst., Nagasaki Univ. Sch. Medicine, Nagasaki, Japan
Rinsho Ketsueki; 22(6):789-791 1981

Bone marrow cells from 13 patients with atypical leukemia were studied cytogenetically using the banding technic. Chromosomal abnormalities were observed in three patients: missing Y, t(8;21), or 5p-with multiple change. Abnormal and normal diploid cells coexisted in all three patients. Cellular aging might have resulted in the loss of the Y chromosome. Clonal evolution of the karyotype could not be seen in 11 patients for whom serial cytogenetic analyses were obtained. (6 Refs) (In JPN)

30. THREE PATIENTS WITH STRUCTURALLY ABNORMAL X CHROMOSOMES, EACH WITH XQ13 BREAKPOINTS AND A HISTORY OF IDIOPATHIC ACQUIRED SIDEROBLASTIC ANEMIA.

Dewald GW, Pierre RV, Phyliky RL
Mayo Clinic, Rochester, MN, 55905
Blood; 59(1):100-105 1982

Structural abnormalities of the X chromosome are rarely found in neoplastic diso rders. We describe three patients with a history of idiopathic acquired sideroblastic anemia (IASA); each one had an abnormal clone of cells in the bone marrow, characterized by a structurally abnormal X chromosome. In two of these patients, the predominant karyotype was 47,X,2idic(X)(q13); in the other patient, it was 46,X,t(X;11)(q13;p15). Inasmuch as all three of these cases involved chromosome band Xq13, as did two previously published cases, we suggest that band Xq13 may be more prone to structural rearrangement than other X chromosome bands in hematologic disorders. The common Xq13 chromosome breakpoint and clinical presentation (IASA) among these three patients and the occurrence of an X-linked type of sideroblastic anemia may suggest that an association exists between X chromosome abnormalities and IASA. Perhaps alteration of a gene or chromosome structure in or near band Xq13 predisposes to development of IASA. The fact that two of these patients had preleukemia and the third had overt acute leukemia may imply that patients with IASA and X chromosome abnormalities have a poor prognosis. Cases of IASA without associated X chromosome abnormalities are known; thus, if an association between IASA and an abnormal X chromosome does exist, most likely it involves only some patients with IASA. (Author abstract) (22 Refs)

31. MARKED KARYOTYPE ABNORMALITIES IN TWO CASES OF ACUTE MYELOGENOUS LEUKEMIA.

Sessarego M, Canepa L, Grammenu S, Bianchi Scarra GL, Ajmar F
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Cancer Genet Cytogenet; 4(4):303-309 1981

Two patients with acute myelogenous leukemia with severe chromosome abnormalities are described. The cytogenetic analysis shows the following karyotype: patient No 1: 41,XY,-1,-2,-4,-5,-13,-15,-17,-17,-18,-22,+5 markers; patient No 2: 46,XY,-2,-5,-7,-13,+16,-21,-21,+5 markers. In each patient one set of double minute chromosomes was observed. (Author abstract) (21 Refs)

32. VARIANT PH1 TRANSLOCATIONS IN CML AND THEIR INCIDENCE (MEETING ABSTRACT).

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Department of Cytogenetics, University of Tokyo, Tokyo, Japan
Proceedings of the Japanese Cancer Association 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

A serial cytogenetic study of 103 cases of Ph1-positive chronic myelocytic leukemia (CML) has been performed by banding techniques. The standard Ph1 translocation, ie, t(9;22)(q34;q11) was observed in 100 cases. A variant Ph1 translocation was observed in 3 cases. In one case, leukemic cells contained two reciprocal translocation. The two translocations were at a t(3;9) (q21;q34) and a t(17;22) (q21;q11); therefore a Ph1 was masked by a translocation of the delected material from the 17q onto the band q11 of the long arm of a chromosome 22. In the second case, a variant Ph1 translocation involved chromosomes 9, 20 and 22, resulting in a karyotype interpreted as: 46, XX, t(9q+;20q+;22q-); in this rearrangement, one of the segments, ie, 9q31 or 9q33 seemed to be interstitially deleted, and inserted into the interstitial region (q11) of a chromosome 20, and the 22q11-qter was translocated onto the 9q. This is the first case in which chromosome 20 was involved in a variant Ph1 translocation. In the third case, the karyotype of leukemic cells was interpreted as: 46, XY, t(5;9;22)(q13;q34;q11). From 15 cytogenetic studies reported as a series of 25 or more cases including the present study, it emerged that the incidence of a variant Ph1 translocation was 4.1% (42/1027 cases of Ph1-positive CML); of the 42, 13 were of a simple type, and 29 were of a complex type. On the present findings and a review of the literature, the importance of the involvement of both chromosomes 9 and 22 in rearrangement, in the genesis of CML, will be discussed. (no Refs)

33. X-RAY INDUCED CHROMOSOME ABERRATIONS IN DOWN LYMPHOCYTES: AN EXPLANATION OF THEIR INCREASED SENSITIVITY.

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Environ Mutagen; 3(1):85-89 1981

Association between altered repair of radiation-induced damage in lymphocytes from two individuals with Down syndrome (trisomy 21) compared with normal cells, and the involvement of the association in increasing chromosome aberration frequencies, were studied. Aberration frequencies in normal and Down lymphocytes were compared following x-irradiation and postirradiation incubation with cytosine arabinoside (ara-C), 5 x 10(-5) M, for 0, 0.5, 1 or 2 hr. Unstimulated Down lymphocytes are more sensitive to the induction of dicentric and ring aberrations by x-rays than normal lymphocytes. X-irradiated cells incubated with ara-C exhibited large increases in aberration frequencies which were proportional to length of exposure to ara-C. Results suggest that the initiation of the repair of damage which is converted into chromosome aberrations is more rapid in Down cells than in normal cells. This could be explained if the total amount of DNA damage which can be converted into aberrations is the same in both cell types but the repair is more rapid in Down cells. Results explain the increased sensitivity of unstimulated lymphocytes from individuals with Down syndrome to the induction of dicentrics by x-rays. The more rapid repair of Down cells results in a higher probability of producing chromosome aberrations and higher aberration frequencies in Down than normal cells. (5 Refs)

34. THE MYELOPROLIFERATIVE REACTION IN A CHILD WITH DOWN SYNDROME: CYTOLOGICAL AND CHROMOSOMAL EVIDENCE FOR A TRANSIENT LEUKEMIA.

Lazarus KH, Heerema NA, Palmer CG, Baehner RL
Dept. Pediatrics, James Whitcomb Riley Hosp. for Children, 1100 W. Michigan St., Indianapolis, IN, 46223
Am J Hematol; 11(4):417-423 1981

Infants with Down syndrome occasionally develop marked myeloproliferative reactions (MPR) indistinguishable from acute myelocytic leukemia but which spontaneously regress. Most authors have attributed MPR to immature or defective control on bone marrow development. In this report serial cytomorphologic and chromosomal findings in the bone marrow and peripheral blood of a child with the MPR suggests that MPR may be due to a spontaneously regressing clone of malignant cells. At the height of the myeloproliferative response, chromosomal studies demonstrated a clone of blast-like cells with a 21-22 translocation consistent with Down Syndrome and an X-8 translocation which was present only in the initial peripheral blood analysis harvested at 24 hr but was not present in the 72 hr samples. This X-8 translocation was not demonstrated in bone marrow or peripheral blood samples obtained at random times throughout the 1 yr followup. During this period there was complete resolution of the MPR. In addition the chromosomes from one cell demonstrated several double minutes at the time of the MPR. Double minutes have previously been reported only in malignant diseases, especially tumors of neural origin and leukemia. These findings raise questions about the benign origin of the MPR and support the idea the MPR may be the result of a spontaneously regressing clone of malignant cells. (Author abstract) (22 Refs)

35. 14Q12 TRANSLOCATION IN A NON-BURKITT LYMPHOMA.

Miyamoto K, Hayashi K, Tsubota T, Tanaka T
Div. Pathology, Cancer Inst., Okayama Univ. Medical Sch., Okayama, Japan
Acta Med Okayama; 35(4):285-287 1981

Chromosome analysis was performed on cells from a patient of null cell lymphoma, well-differentiated type. A 14q12 translocation was observed in all the banded cells. In addition, there were multiple chromosome abnormalities. This case will be useful in considering the significance of the 14q1(1-3) translocation in malignant lymphoma disease. (Author abstract) (7 Refs)

36. CHARACTERISTICS OF A BRAIN LYMPHOMA CELL LINE DERIVED FROM PRIMARY INTRACRANIAL LYMPHOMA.

Miyoshi I, Kubonishi I, Yoshimoto S, Hikita T, Dabasaki H, Tanaka T, Kimura I, Tabuchi K, Nishimoto A
Dept. Medicine, Kochi Medical Sch., Kochi 781-51, Japan
Cancer; 49(3):456-459 1982

A brain lymphoma cell line, designated TK, was established from biopsy material of a patient with primary intracranial lymphoma. The TK cell line grew in suspension with clumps of cells and consisted of primitive lymphoid cells. TK cells and original lymphoma cells from which the cell line was derived bore surface immunoglobulin and lacked Epstein-Barr virus-determined nuclear antigen. Transpl antation of the TK cells into immunosuppressed newborn hamsters gave rise to invasive growth of tumors with metastasis to the brain and eyes. These findings provide evidence for a B-cell origin of the brain lymphoma in this case. (Author abstract) (13 Refs)

37. PREDICTABILITY OF IMMUNOLOGIC PHENOTYPE BY MORPHOLOGIC CRITERIA IN DIFFUSE AGGRESSIVE NON-HODGKIN'S LYMPHOMAS.

Jaffe ES, Strauchen JA, Berard CW
Lab. Pathology, NCI, Building 10, Room 2N110, Bethesda, MD, 20205
Am J Clin Pathol; 77(1):46-49 1982

Diffuse aggressive non-Hodgkin's lymphomas are immunologically and morphologically heterogeneous. Morphologic subclassifications have been proposed with a presumptive relationship to immunologic phenotype. Six histologic types were studied, four of presumed follicular origin (large cleaved, large non-cleaved, mixed follicular center cell, and blastic) and two of presumed nonfollicular origin (pleomorphic pyroninophilic and pleomorphic convoluted). Two of these follicular subtypes were found to be associated with the frequent presence of B-cell markers; large non-cleaved, six of seven; and blastic, four of six. However, four of nine T-cell lymphomas were misclassified as lesions of follicular center cell type, indicating the difficulty of distinguishing some convoluted cells of T-cell lymphoma from irregularly cleaved cells of follicular lymphoma. Pleomorphic pyroninophilic or B-immunoblastic morphology was associated with B-cell markers in only two of six cases; two additional cases had T-cell markers, one had histocytic markers and in one case, no markers were demonstrable. Thus, this morphology may reflect a common pathway of transformed lymphoid cells. Some cases of T-cell origin could be recognized by the striking pleomorphic convoluted histology (3 of 5 cases) but morphologic overlap with pleomorphic B-cell tumors, particularly transformed nodular lymphomas, posed a problem. This histopathologic subclassification correct-

ly predicted immunologic phenotype in only 61% of cases, suggesting that in diffuse non-Hodgkin's lymphomas, histologic appearance alone may not be a reliable indicator of immunologic surface markers. (Author abstract) (17 Refs)

38. CYTOGENETIC STUDIES OF HAIRY CELL LEUKEMIA.

Lele KP, Filippa DA, Chaganti RS
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Cancer Genet Cytogenet; 4(4):325-330 1981

Mononuclear cells from peripheral blood and spleen of four patients with hairy cell leukemia (HCL) were cultured for 1 to 10 days with and without phytohemagglutinin (PHA) stimulation. Blastogenesis and mitoses were not observed in the unstimulated cells cultured for up to 3 days. Prolonging the culture time of unstimulated cells to 7 days produced blastogenic response; a further increase i n culture time to 10 days showed transformed cells but not mitoses. Poor PHA response was noted in the cultures stimulated for 3 days, but cells cultured for 7 days and then stimulated with PHA entered mitosis. Surface immunoglobulins were exhibited in 78-94% of the cells in the blood and spleen of patients. In addition, these cells had tartrate-resistant acid phosphatase and were able to phagocytize latex particles by which properties they were identified as hairy cell leukemia cells. Chromosome abnormalities were present in a proportion of cells of each patient, none of them, however, were clonal. (Author abstract) (12 Refs)

39. CLONAL CHARACTERISTICS OF CUTANEOUS T CELL LYMPHOMAS: CYTOGENETIC EVIDENCE FROM BLOOD, LYMPH NODES, AND SKIN.

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Dept. Pathology/G3, Sch. Medicine, Univ. Pennsylvania, Philadelphia, PA, 19104
J Invest Dermatol; 78(1):69-75 1982

Chromosome studies were done on mitogen-stimulated lymphocytes from one or more tissues (blood, lymph nodes, skin lesions) in 15 patients with mycosis fungoides or Sezary syndrome. A cytogenetically abnormal clone was found in 10 individuals, including 6 with data from several tissues. In four cases the same aberrant clone was identified in a skin lesion as well as in blood and/or lymph node. the abnormal chromosome patterns ranged from hypodiploid to hypertetraploid, and there was no evidence of unrelated karyotypically-altered lines at different sites. A 6q- chromosome, previously reported in acute lymphocytic leukemia, was found in two patients. The results support the concept that cutaneous T cell lymphomas (CTCL) are clonal disorders, presumably unifocal in origin, with the skin lesions populated by cells from the same neoplastic clone that involves lymph nodes and blood. (Author abstract) (17 Refs)

40. SISTER CHROMATID DIFFERENTIATION: A NEW CYTOGENETIC METHOD FOR THE MEASUREMENT OF CELL CYCLE TIME IN LEUKEMIAS (MEETING ABSTRACT).

Becher R, Schmidt CG
West German Tumor Center, Innere Universitatsklinik, 4300 Essen 1, W. Germany
UICC Conference on Clinical Oncology, October 28-31, 1981, Lausanne, Switzerland. International Union Against Cancer 131 pp., 1981.

After incubation of cells in 5-bromodeoxyuridine (BrdU) containing medium in vitro, a typical differentiation of sister chromatids (SCD) can be observed in metaphases which have passed more than two cell cycles during a given culture time. This different staining is caused by either unifilar or bifilar substitution of the thymidine analog BrdU corresponding to the semiconservative replication of DNA and allows the identification of metaphases which have passed one (M1), two (M2) or three (M3) cell cycles. Marker chromosomes can be used for the diagnosis of malignant cell clones. Here, we report on eight cases of un treated acute leukemia (AL). The distribution pattern of M1, M2 and M3 metaphases was compared with that of six normal bone marrows. In most of the acute leukemias a shift from M3 to M2 and an accumulation of M1 metaphases was observed. Cells able to pass three complete cycles (calculated cell cycle time less than 16 hr) during the culture time of 50 hr were rare or absent in AL, indicating that leukemic cells apparently divide more slowly than normal bone marrows, which is in good agreement with results obtained by autoradiographic methods. Up to 96% of leukemic cells did not pass more than one cell cycle within 50 hr. (no Refs)

41. FAMILIAL TRANSLOCATION DETECTED THROUGH A CHILD WITH ACUTE LYMPHOCYTIC LEUKAEMIA (MEETING ABSTRACT).

Tsenghi C, Dentaki-Svolaki C, Haidas S, Metaxotou C, Zannos-Mariolea L
1st Department of Paediatrics, Athens University Research Laboratory Unit of Cytogenetics and Unit of, Haematology Athens, Greece
Sixth Meeting of the International Society of Haematology, European and African Division, August 30-September 4, 1981, Athens, Greece. Hellenic Society of Haematology 409 pp., 1981.

Chromosome changes in cells of patients with acute leukemia have recently been shown to have diagnostic and prognostic significance. We report on a five-year old patient with acute lymphocyte leukemia (ALL) who was found to have a balanced translocation of the genetic material. His karyotype was 46, XY, t(6;17) (p11;q25) both in direct bone marrow preparations and in peripheral blood WBC cultures. Since this translocation involved chromosomes not usually associated with leukemia we examined other members of the patient's family. The same structural rearrangement was found in the patient's father and a brother. The possible correlation between the chromosomal abnormality in this patient and the development of the disease is discussed. (no Refs)

42. DECREASED TUMORIGENICITY OF RODENT CELLS AFTER FUSION WITH LEUKOCYTES FROM NORMAL AND LEUKEMIC DONORS.

Geurts van Kessel AH, De Boer WC, Van Agthoven AJ, Hagemeijer A
Dept. Cell Biology and Genetics, Erasmus Univ., Rotterdam, The Netherlands
Somatic Cell Genet; 7(6):645-656 1981

Hybrid cell lines, derived from fusion of tumorigenic rodent cells (mouse Pg 19 or Chinese hamster a3) with WBC from leukemic donors were isolated and tested for growth in congenitally athymic nude mice. Cytogenetic analysis, using banding techniques, was performed on cells before injection and on the tumors which eventually developed. Pg 19 mouse cells alone were highly tumorigenic; 1 x 10(5) cells resulted in 100% tumors. The a3 grew more slowly and 2 x 10(6) cells were needed to produce tumors in 75% of mice in 10 days. WBC from chronic myeloid leukemia donors, with inocula of up to 4 x 10(7) cells, failed to form tumors within 3 mo in nude mice, further immunosuppressed by ip cyclophosphamide. The chromosome analyses did not reveal a human chromosome-bearing

factor(s) which singly appeared responsible for the tumor suppression. The presence of the Philadelphia translocation in the leukemic cells does not appear to have deprived these cells of their tumor-suppressing ability. (29 Refs)

BIOCHEMICAL, IMMUNOLOGICAL AND OTHER CELL BIOLOGY STUDIES

43. T-CELL GROWTH FACTOR (INTERLEUKIN 2) CONTROL OF T-LYMPHOCYTE PROLIFERATION: POSSIBLE INVOLVEMENT IN LEUKEMOGENESIS.

Gillis S, Mertelsmann R, Moore MA
Basic Immunology Program, Fred Hutchinson Cancer Res. Center, 1124 Columbia St., Seattle, WA, 98104
Transplant Proc; 13(4):1884-1890 1981

Isolation of murine and human leukemic T-cell lines that produce exceptionally high quantities of interleukin 2 (IL-2), and screening of freshly isolated patient-derived human leukemic blasts for IL-2 production and response capabilities, are described. An IL-2 microassay was used to screen fractions of biochemically manipulated, conditioned medium for the capacity to promote sustained in vitro proliferation of murine cytotoxic T-lymphocytes. Two leukemic cell lines, murine LBRM-33 and human Jurkat-FHCRC, produced large quantities of IL-2 upon stimulation with phytohemagglutinin (PHA). Both of the cell lines bear conventional T-cell markers and phenotypic markers indicative of immature cell type. Analysis of leukemic blast cell response of mononuclear blood cells from patients with various leukemias revealed consistent IL-2 production and response patterns. All patients who exhibited high levels of deoxynucleotidyl transferase (TdT) in leukemic blood cells showed a small proliferation increase in response to PHA stimulation but produced exceptionally high levels of IL-2. The response to added purified human IL-2 and PHA was atypical in most patients, in that incorporation of 3H-thymidine decreased in the majority of TdT+ leukemias when compared to PHA-stimulated proliferation. Such a finding was in marked contrast to results obtained with normal lymphocytes. IL-2 production and use, responses and TdT expression in leukemic cells are discussed. (17 Refs)

44. A T-CELL LINE DERIVED FROM NORMAL HUMAN CORD LEUKOCYTES BY CO-CULTURING WITH ADULT T-CELL LEUKEMIA (ATL) CELLS: IMMUNOFLUORESCENT AND ELECTRON MICROSCOPIC STUDIES (MEETING ABSTRACT).

Miyoshi I, Yoshimoto S, Kubonishi I, Shiraishi Y, Akagi T, Ohtsuki Y, Hinuma Y
Department of Medicine, Kochi Medical School, Kochi, Japan
Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

ATL cells from a female patient and cord WBC from a normal male infant were co-cultured and a T-cell line (MT-2) of cord WBC origin was established. The MT-2 line was E+, EA-, EAC-, SIg- , anti-T+, Ia+ and EBNA-. MT-2 cells had a normal male karyotype but were tumorigenic in newborn hamsters. The majority of MT-2 cells were reactive with sera from ATL patients in indirect immunofluorescence. Electron microscopy of MT-2 revealed numerous C type virus particles in the extra-cellular spaces. The origin and role of the virus in transformation of normal human cord T-cells and currently under investigation. (no Refs)

45. A T-CELL LINE DERIVED FROM NORMAL HUMAN CORD LEUKOCYTES BY CO-CULTURING WITH HUMAN LEUKEMIC T-CELLS.

Miyoshi I, Kubonishi I, Yoshimoto S, Shiraishi Y
Dept. Medicine, Kochi Medical Sch., Oko-cho, Nank. ku-shi, Kochi-ken 781-51, Japan
Gan; 72(6):978-981 1981

A unique T-cell line, MT-2, was established from normal human cord leukocytes of a male infant by co-culturing with leukemic T-cells from a female patient with adult T-cell leukemia. MT-2 cells expressed receptors for sheep erythrocytes and complement and were reactive with anti-T-cell and anti-Ia sera. They were negative for Fc receptors, surface immunoglobulin, and Epstein-Barr virus nuclear antigen. Chromosomally, the MT-2 line was male and most cells were shown to have a normal diploid karyotype. The cultured cells were tumorigenic when transplanted into immunosuppressed newborn hamsters. (Author abstract) (11 Refs)

46. HUMAN ERYTHROID CELL LINES DERIVED FROM A PATIENT WITH ACUTE ERYTHREMIA.

Okano H, Okamura J, Yagawa K, Tasaka H, Motomura S
Dept. Pathology, Kyushu Cancer Center Res. Inst., 595 Notame, Minami-ku, Fukuoka 815, Japan
J Cancer Res Clin Oncol; 102(1):49-55 1981

Three continuous human cell lines, designated KMOE, derived from a patient with acute erythremia (Di Guglielmo's disease) are reported. The cell lines are the cultures of (1) bone marrow cells, (2) peripheral blood cells, and (3) cells from a tumor developed into an athymic nude mouse after transplantation of the cultured bone marrow cells. Cells of all three lines show morphology of immature erythroblast and have i(17q) marker chromosome. They are negative for both Philadelphia chromosome and Epstein-Barr virus nuclear antigen. Although all KMOE cells in suspension culture are benzidine-negative, benzidine-positive cells are found within colonies formed in semi-solid culture media. The relative number of colonies with benzidine-positive cells is increased when sodium butyrate is added to the culture. The KMOE cell lines are human erythroid cell lines with erythroblastic morphology and still retain their tendency for differentiation. (Author abstract) (9 Refs)

47. STUDIES ON THE COLONY FORMATION OF LYMPHOBLASTOID CELL LINES.

Luan Q, Zhang D, Yan M
Dept. of Microbiology, Shanghai Second Medical Coll., Shanghai, People's Republic of China
Zhonghua Weishengwuxue He Mianyixue Zazh; 1(2):113-117 1981

It has been shown that on soft agar medium coloning efficiencies are different for normal and neoplastic lymphoblastoid cells, even though they may have similar morphological and biological characteristics. Cloning efficiencies are described for the following three cell lines: (1) normal human peripheral lymphoblastoid cell line (H26), (2) EB virus transformed cell line (B95-8), and (3) Burkitts' lymphoma (Raji) cell line. The cloning efficiencies for H26 were 0.07-0.5%, and for B95-8 and Raji cell lines were 11.35-30.58% and 26.4-48.84%, respectively. (11 Refs) (In CHI)

48. THE RIDDLE OF HODGKIN CELLS.

Diehl V
Abt. Hamalotogie, Medizinische Hochschule Hannover, Hannover, W. Germany
MMW; 123(48):1827-1828 1981

Characteristics of the first tumor cell cultures successfully established from biopsy material of patients with Hodgkin's disease are described. Testing for markers of differentiation revealed that the cell lines had antigenic properties similar to those of early myelo-monocytes. Although the cell lines were established from biopsy specimens of four patients, they possessed many identical characteristics, identical marker chromosomes, and common cytochemical features. One of the four cell lines was positive for an Epstein-Barr-virus (EBV)-induced antigen, and another cell line possessed EBV receptors. The cell lines were poor inducers of tumor growth in nude mice. (no Refs) (In GER)

49. FUNCTIONAL STUDIES ON B CELLS IN HUMAN BONE MARROW: IN VITRO MITOGEN STIMULATION OF NORMAL AND MALIGNANT B CELLS.

Hammarstrom L, Smith CI, Pettersson D, Mellstedt H, Holm G
Dept. Immunobiology, Wallenberg-laboratory, Karolinska Inst., Lilla Frescati, S-104 05 Stockholm 50, Sweden
Clin Exp Immunol; 43(1):157-164 1981

Using the protein A plaque assay, bone marrow cells from normal donors were shown to secrete spontaneously immunoglobulins mainly of the IgG and IgA class. After mitogenic activation, a marked increase in IgM production was observed with kinetics and cell density requirements similar to that of blood lymphocytes. In Morbus Waldenstrom patients, IgM was the predominant Ig class secreted spontaneously by bone marrow cells. The high in vitro background proliferation of these cells could be abolished by addition of the appropriate anti-idiotypic antiserum. After stimulation with mitogens, differentiation of cells within the malignant clone to immunoglobulin-secreting lymphocytes was evidenced, suggesting a retained responsive capacity of the transformed cells. (Author abstract) (27 Refs)

50. RECEPTOR ACTIVITIES FOR LOW-DENSITY LIPOPROTEIN AND ACETYLATED LOW-DENSITY LIPOPROTEIN IN A MOUSE MACROPHAGE CELL LINE (IC21) AND IN HUMAN MONOCYTE-DERIVED MACROPHAGES.

Traber MG, Defendi V, Kayden HJ
Dept. Medicine, New York Univ. Medicine, New York, NY, 10016
J Exp Med; 154(6):1852-1867 1981

Lipoprotein and cholesterol metabolism in the mouse macrophage cell line IC21 (Simian virus 40-transformed peritoneal macrophages) was compared with that of human monocyte-derived (HMD) macrophages. IC21 macrophages exhibited detectable low-density lipoprotein (LDL) receptor activity; they degraded acetylated LDL (AcLDL) with high affinity. Saturation curves of 125I-AcLDL degradation by IC21 macrophages and mouse peritoneal macrophages were virtually superimposable. The 125I-AcLDL binding site on IC21 macrophages recognized dextran sulfate: the rates of 125I-AcLDL and 125I-LDL degradation were reduced 5-and 10-fold, respectively, in the presence of 5 ug/ml dextran sulfate. IC21 macrophages showed lower levels of high-affinity LDL degradation and greater capacity to degrade AcLDL than did HMD macrophages. When IC21 cells were incubated with lipoprotein-depleted serum (LPDS), cellular cholesterol content was decreased and the rate of sterol synthesis was markedly increased. Data suggested that IC21 macrophages were able to use AcLDL cholesterol in place of endogenously synthesized cholesterol; LDL cholesterol also entered the cells but at a slower rate and thus did not provide cholesterol in sufficient amounts to inhibit cholesterol synthesis completely. Further evidence that uptake of LDL via the LDL receptor pathway does not provide sufficient cholesterol to the IC21 macrophages was gained from comparison of cholesteryl ester synthesis by IC21 and HMD macrophages. Results indicated that all aspects of lipoprotein and cholesterol metabolism studied are similar for IC21 and mouse peritoneal macrophages. Thus IC21 macrophages are an acceptable model system for study of lipoprotein and cholesterol metabolism. (35 Refs)

51. SURFACE GLYCOPROTEINS OF NORMAL AND MALIGNANT HEMATOPOIETIC CELLS.

Andersson LC
Pathology Inst., Helsinki Univ., 00290 Helsinki 29, Finland
Duodecim; 97(18):1509-1518 1981

Surface glycoprotein (GP) analysis was used to classify normal and malignant hematopoietic cells and to measure their degree of differentiation; the technique may be of importance in the prognosis and treatment of various types of leukemia. When GP120 becomes GP130 in the conversion of T-lymphocytes to killer cells, a definite change occurs in glycosylation, altering electrophoretic mobility. GP130 is specifically bound to the lectin of Vicia villosa, but the lectin does not react with GP120. When the promyelocyte grows into a granulocyte, the disappearance of GP160 and the appearance of GP130 is an example of altered glycosylation. Since GP160 and GP130 both react to the same antiserum, they clearly possess a common peptide component. Changes linked to differentiation during the glycosylation of surface glycoproteins can lead to the formation of differentiation antigens, important indicators of interaction between cells. A considerable part of the genetic information that measures surface changes in the cell during growth could be transmitted by way of various carbohydrate transferases. (22 Refs) (In FIN)

52. ANTIBODIES AGAINST FELINE AND GIBBON APE REVERSE TRANSCRIPTASE ON SURFACE OF SPLEEN CELLS IN HUMAN MYELOGENOUS LEUKEMIA.

Jacquemin PC
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Eur J Cancer Clin Oncol; 17(12):1283-1286 1981

We reported that antibody bound to blood leukocytes of patients in chronic myelogenous leukemia neutralize reverse transcriptase. The specificity of neutralization depended on the phase of the disease. Antibody bound to chronic phase leukemia cells neutralized Gibbon Ape leukemia virus reverse transcriptase, while that bound to blastic phase cells neutralized Feline leukemia virus reverse transcriptase. Spleen cells obtained from patients with chronic myelogenous leukemia have surface-bound immunoglobulins that recognize both reverse transcriptases. These data in the spleen suggest the existence of a progressive shift in cell population from a chronic phase type cell to a blastic phase type cell. (Author abstract) (9 Refs)

53. ANTI-POLY(A) POLYMERASE ANTIBODIES IN SERA OF TUMOR-BEARING RATS AND HUMAN CANCER PATIENTS.

Stetler DA, Rose KM, Jacob ST

Dept. Pharmacology and Specialized Cancer Res. Center, Milton S. Hershey Medical Center, Pennsylvania State Univ., Hershey, PA, 17033

Proc Natl Acad Sci USA; 78(12):7732-7736 1981

Poly(A) polymerase (polynucleotide adenylyl-transferase; ATP:polynucleotide adenylyltransferase, EC 2.7.7.12) was covalently linked to diazobenzyloxymethyl-filters and used to screen the sera from a number of tumor-bearing rats and human cancer patients for antibodies to poly(A) polymerase. Sera from rats that had been inoculated with any of several Morris hepatomas or a mammary adenocarcinoma contained immunoglobulins capable of complexing with poly(A) polymerase. No antibodies to the enzyme could be detected in sera from control animals or from those bearing tumors for short periods of time. Antibodies to poly(A) polymerase were also observed in sera from human patients with leukemia, polycythemia vera, and Wilms tumor. The antibodies were not evident in sera from normal volunteers or from patients with nonneoplastic diseases. These included lupus erythematosus, a disorder in which antibodies are produced against an array of nuclear proteins. Immunoglobulins from the serum of one of the human patients were capable of inhibiting poly(A) polymerase activity in vitro, whereas those prepared from the serum of a normal volunteer did not affect enzyme activity. As determined by the diazobenzyloxymethyl-filter technique, the relative concentration of antibodies in the sera of an individual with leukemia (in remission) increased s everalfold during a relapse. These data suggest that the presence of antibodies to poly(A) polymerase may be characteristic of sera from cancer patients and that the relative concentration of these antibodies may be indicative of the disease state. (Author abstract) (26 Refs)

54. EVALUATION OF CARCINOEMBRYONIC ANTIGEN (CEA) IN PATIENTS WITH HEMATIC CANCER.

Bulfoni A

II Divisione Medica, Ospedale Civile di Udine, Udine, Italy

Arch Sci Med (Torino); 138(4):449-454 1981

Carcinoembryonic antigen (CEA) was evaluated in 47 patients with non Hidgkin's lymphoma 12, Hodgkin's lymphoma (HL) 9, chronic lymphatic leukemia (CLL) 6, chronic myeloid leukemia (CML) 3, plasmacytoma (PC) 6, idiopathic myelofibrosis 2, polycythemia vera 2, and 21 patients with cancers of endodermal tissues (gastric 8, bronchogenic 7, pancreatic 4, and colorectal 2). The CEA determinations were performed using radioimmunoassay. Of 47 patients with hematic cancer, 10 had CEA values above 20 nanog/ml. These 10 patients had HL (4), CLL (2), PC (2), non HL (1), and CML (1). The highest value of CEA (320 nanog/ml) was observed in one case of CLL, which was complicated with primary hepatic carcinoma. The CEA values were negative in 37 (79%) of 47 patients and independent of the phase of the disease. Of the 21 patients with cancers of entodermal tissues, 76% had CEA values above 20 nanog/ml, and quantitatively the CEA values were higher than in the 10 hematic cancer patients. (35 Refs) (In ITA)

55. CONTRASTING PATTERNS OF PROTEIN KINASE ACTIVITIES AMONG NORMAL PERIPHERAL BLOOD LYMPHOCYTE SUBPOPULATIONS AND LYMPHOID CELL LINES.

Elias L, Longmire J, Bankhurst AD

Cancer Res. and Treatment Center, University New Mexico, Albuquerque, New Mexico, 87113

J Lab Clin Med; 99(1):56-63 1982

Human peripheral mononuclear cell suspensions were separated into E-rosette-positive (T cell) and E-rosette-negative (non-T cell) fractions and assayed for cAMP binding activity and histone and casein kinase activity, in the presence and absence of cAMP. Each of these activities was higher in E-rosette-positive than E-rosette-negative fractions. Cyclic AMP binding and histone kinase activities were further noted to be higher in T lymphoblastoid cell lines when compared to lines of non-T lymphoid cell origin. In addition, DEAE-cellulose chromatography revealed a qualitative contrast of isoenzymic composition of protein kinase from these cell lines. Cyclic AMP-independent casein kinase activity was high in both types of cell lines. These results suggest that high protein kinase activity is characteristic of T cells and may be related to their higher sensitivity to cAMP agonists in comparison to non-T cells. This study also provides further evidence for an association between increased cAMP-independent protein kinase activity and the transformed state, which has been noted for a variety of other cell types. (Author abstract) (30 Refs)

56. RED CELL ENZYMES IN PRELEUKAEMIA (MEETING ABSTRACT).

Lintula R, Hekali R, Borgstrom GH, Vuopio P

III Department of Medicine, University of Helsinki, Helsinki, Finland

Sixth Meeting of the International Society of Haematology, European and African Division, August 30-September 4, 1981, Athens, Greece. Hellenic Society of Haematology 409 pp., 1981.

Red cell enzymes were studied in 25 patients with preleukemia. Five of these patients had normal bone marrow karyotype, 5q-syndrome was noted in six patients, 12 patients had other abnormalities and two had constitutional anomaly. Parameters studied included hexokinase (HK), glucosephosphate isomerase (GPI), phosphofructokinase (PFK), aldolase (ALD), triosephosphate isomerase (TPI), glyceraldehyde-3-phosphate dehydrogenase (GAPD), phosphoglycerate kinase (PGK), diphosphoglyceromutase (DPGM), monophosphategiyceromutase (MPGM), enolase (ENOL), pyruvate kinase (PK), lactate dehydrogenase (LD), glucose-6-phosphate dehydrogenase (G-6-PD), 6-phosphogluconate dehydrogenase (6-PGD), adenylate kinase (AK), aspartateaminotransferase (ASAT), ATPase, glutathione reductase (GR), glutathione (GSH), ATP and 2,3-diphosphoglycerate (2,3-DPG). Abnormalities in red cell enzymes were common. All patients had some abnormalities and usually the enzyme activities were increased. Most consistent findings were increased HK, ENOL, 6-PGD, GAPD, ALD, G-6-PD, LD, ATPase and DPGM activities, high GSH level and low ATP level. Abnormalities in red cell enzymes were not associated with any specific chromosomal aberration. (no Refs)

57. ON THE DYNAMICS OF ABRIN BINDING TO RECEPTOR SITES IN NORMAL AND EPSTEIN BARR VIRUS TRANSFORMED LYMPHOCYTE CELL CULTURES.

Witten M, Bennett CE, Glassman AB, Gordon I
Dept. Matnematics, Univ. California, Santa Barbara, CA, 93105
J Recept Res; 2(2):175-201 1981

The effects of treatment with varying doses of abrin, a toxic D-galactose binding lectin, on DNA protein and synthesis of normal and Epstein Barr Virus (EBV)-transformed lymphocytes were investigated. Activation, stimulation, and relative toxicity factor indices were studied. Possible relationship between DNA and protein synthesis rates measured by simultaneous tritiated thymidine (3H-TdR) and (14C)leucine uptake were also studied. Receptor sites were determined with the use of 125I-abrin. Three repeated cell counts were made for each cell type, for each dose and time pair, and for each cell density and metabolic pair. Abrin is a metabolic toxin for the EBV-lymphocyte population and has also some effect on the normal cell population. The EBV-transformed lymphocyte population is heterogeneous with three major lymphocyte subpopulations, each with a different number of receptor binding sites for abrin. Assuming that the size o f the abrin receptor site is a fixed constant across the different morphological subpopulations, then the number of sites capable of being packed on the cell surface is a function of the cell surface area. The mean number of receptors bound/EBV-lymphocyte exerting biological influence is in the interval 59,264-370,040 receptors/cell. Theoretical and experimental results showed a significant resemblance. (16 Refs)

58. ANALYSIS OF THE DRW6 COMPLEX IN THE JAPANESE POPULATION.

Akaza T, Suchi T, Morimoto T, Takagi H, Awashima F, Yoshida TO, Kamura H
Dept. Clinical Lab., Aichi Cancer Center Hosp., Aichi, Japan
Transplant Proc; 13(4):1983-1984 1981

Through the use of sera from pregnant Japanese women a new D-locus (DR) antigen has been identified in the Japanese population. MT2-positive cell panels were separated into four components, other than DRw8, using anti-DR5 and -DRw6 sera. One component, DR5, was clearly defined by serum AK-7. The second consisted of cells that reacted with AH-3 and B-4, but did not react with AK-7; it included two specificities, termed DRw6.2(3) and Q51, which are tentatively named 5L. Another component, AB-2 reacted with 5L and DRw8 but not with DR5.5L and was included in MT2 and MT4. The residual components were related to DRw6.1 and DRw6Y and were tentatively called 6L. Another submitted serum, F-6 had almost the same specificity as the anti-MT2 reagent but some MT2-positive cells failed to react to F-6, suggesting the presence of an additional or new DR antigen, Q6. A family study is described in which Q6 was inherited by children from the father. Child 2 had acute monocytic leukemia; when his B cells were cultured as a B-cell line, the cultured cells showed the same reaction pattern to Q6 as the donor's peripheral B lymphocytes. No linkage disequilibrium between Q6 and the human WBC antigen-A, B, C locus antigens was observed. Such studies permitted the DRw6 complex to be split into three 'antigens', Q6, 5L, and 6L, having a phenotype frequency of 6.3%, 7.4%, and 35.5%. (5 Refs)

EXPERIMENTAL STUDIES INVOLVING CHEMICAL AGENTS AND IRRADIATION

59. A SURVEY OF PATHOLOGICAL CHANGES ASSOCIATED WITH LONG-TERM HIGH TAR TOBACCO SMOKE EXPOSURE IN A MURINE MODEL.

Keast D, Ayre DJ, Papadimitriou JM
Dept. Microbiology, Queen Elizabeth II Medical Centre, Univ. Western Australia, Nedlands, Western Australia, 6009, Australia
J Pathol; 135(4):249-257 1981

Long-term effects of exposure to tobacco smoke (TS) were studied in inbred female BALB/c mice. A total of 117 mice were exposed to smoke of 30 high-tar cigarettes (16 mg tar, 1.1 mg nicotine/cigarette) for 7-8 min/day, 5 days/wk for 95 wk. Exposure was interrupted for 3 wk between the 48th and 49th wk of exposure. Compared to a group of 130 controls, mice exposed to TS showed a significant rise in mortali ty after approx 79 wk. Relative mortality in TS-exposed mice was 1.7x that in controls after 83 wk. Occurrence of bronchial adenoma in TS-exposed mice was 3.8x that in controls at 83 wk; occurrence of lymphomas was 2.6x that in controls at 83 wk. Examination of various organs showed that TS-exposed mice were protected from ovarian and paraovarian hematomas and liver lesions. Examination of lungs showed that, although lesions occurred in both groups, TS-exposed mice were more seriously compromised. Moderate to severe interstitial pneumonia was found in 75% of TS-exposed mice and 25% of controls. Results indicate that long-term exposure to TS increases the rate of occurrence of pulmonary neoplasms in mice, and that responses of mice to TS differ significantly in some respects from responses of humans to TS. (15 Refs)

60. RESIDUAL DAMAGE IN HEMATOPOIETIC CELLS FOLLOWING A SINGLE DOSE ADMINISTRATION OF METHYL NITROSOUREA (MEETING ABSTRACT).

Inoue T
Department of Pathology, Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan
Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

To evaluate residual damage from leukemogenic agents, capabilities of proliferation in hematopoietic stem cells (CFUs) in mice treated iv with a single leukemogenic dose (50 mg/kg body wt) of methyl nitrosourea (MNU) were examined by means of spleen colony assay, 3H-thymidine cytocide, 125 iodo-deoxyuridine incorporation into spleen and bone marrow in fatally irradiated mice transfused with 4.5 x 10(6) bone marrow cells from treated mice. Mice given MNU and kept for 3 wk were compared with a group, which had been kept for 3 days after the administration of MNU, for acute toxicity. No significant changes were observed between control and MNU-treated mice kept for 3 wk, in total bone marrow cells, number of CFUs per femur or unit number of cells, and thymidine cytocide rate of the CFUs-pool. Significant change, however, was observed in the proliferation capability of CFUs. (no Refs)

61. ONCORNA VIRUSES IN N-METHYL-N-NITROSOUREA-INDUCED LYMPHOMAS IN MICE.

Pinter A, Borzsonyi M, Torok G, Surjan A, Csik M
Orszagos Kozegeszsegugyi Intezet, Budapest, Hungary
Magy Onkol; 25(4):227-235 1981

Fifteen newborn (C57BL/6xDBA/a) F1 (BDF1) hybrid mice were treated with N-methyl-N-nitrosourea (MNU: 20 mg/kg ip). Five of the 15 animals developed thymic lymphomas, identified histologically and immunologically as lymphoblastic lymphomas, during the 145-day observation period, but no tumors were found in the 20 control animals treated with physiological saline soln only. Unlike the thymic cells of the young control animals, the tumor cells produced oncorna viruses growing in murine tissues only. According to their protein expression, the endogenous, N-tropic viruses represent a homogeneous population. Similar virus was found in thymic cells of a 5-mo-old mouse, which suggests the possibility of age-dependent, spontaneous activation. Since spontaneous lymphoma does not occur in BDF1 mice under the age of 1.5 yr, the viruses isolated are probably not oncogenic, but possess a tumor-promoting property. (19 Refs) (In HUN)

62. TRANSFORMING RNA: CONSIDERATIONS ON THE MECHANISM OF LEUKEMOGENESIS IN MICE (MEETING ABSTRACT).

Hamada K, Yanagihara K, Kajitani T, Kamiya K, Seyma T, Yokoro K
Department of Pathology, Hiroshima University, Hiroshima, Japan
Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

Although the causative implication of a virus in induction of leukemia in mice has long been suspected, a unified concept of leukemogenic mechanism has not been wholly established, due partly to the fact that many mouse strains are naturally infected with C-type RNA retroviruses. Leukemias developed at a high rate in NIH/Swiss mice following administration of N-nitrosoethylurea (NEU). An agent, which transforms cells of several species in vitro and appears to be leukemogenic in collaboration with endogenous MuLV, was isolated from thymi of NEU-induced leukemic mice. The cell transforming capacity of the agent was completely destroyed by treatment with RNase but was not affected by DNase. RNA extracted from SC-1 mouse cells transformed by the agent also showed cell transforming ability. These findings imply that chemical or physical agents exert their leukemogenic activity through the induction of RNA molecules containing transcripts of transforming gene of the cellular origin. (no Refs)

63. TRANSPLANTATION EXPERIMENTS WITH LEUKAEMIA CAUSED BY CHEMICAL CARCINOGENS (MEETING ABSTRACT).

Ember I
University Medical School, Debrecen, Hungary
Ninth Congress of the Haematological Society, October 1-3, 1981, Debrecen, Hungary. The Society 175 pp., 1981.

Bojan and Kertai using urethane and diethylstilbestrol caused acute lymphoid leukemia in C3H/He mg/Lati x AKR/Lati F1 hybrid females, which was also characterized by the tumorous infiltration of the ovaries. Splenic and ovarial cell-suspensions prepared of leukemic animals were used by the author for grafting leukemia into newborn and adult C3H and AKR mice, as well as into newborn and adult R/A rats. In newborn females, (C3H, AKR, R/A) besides leukemia, tumor of the ovary also developed. In adult AKR mice (male and female) only leukemia developed, while adult C3H females developed lymphosarcoma involving both ovaries and lymph nodes. Adult C3H males and R/A rats remained free from leukemia. Significant differences between the effect of the two cell-suspensions couldn't be observed. (no Refs)

64. CHARACTERIZATION OF A LYMPHOMA INDUCED BY BUSULFAN AND CHLORAMPHENICOL IN CAF1 MICE (MEETING ABSTRACT).

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Department of Medicine, Hines Veterans Administration Hospital, Hines, IL, 60141
Tenth Annual Meeting, Midwest Autumn Immunology Conference, Oct 18-20, 1981, Minneapolis, Minnesota University of Minnesota; 1981

We previously showed that injection of Busulfan and chloramphenicol into CAF1 mice induced the development of T-cell lymphoma in 50% of the mice. The lymphoma cells from the spleen were transplantable into other normal CAF1 mice by intravenous, intraperitoneal, or sc injection. In the recipients the lymhoma cells infiltrated spleen, thymus, and lymph nodes. The sc injection of the cells resulted in subcutaneous nodules with late infiltration of the spleen. The cells from the nodules expressed Thy 1.2 alloantigen and brain associated antigen. None of the Lyt antigens (Lyt 1.1, 1.2 or 2.2) were expressed on the lymphoma cells. The primary sheep cell immune responses of these lymphoma mice were found to be normal. These studies indicate that the lymphoma induced by Busulfan and chloramphenicol are transformed early T cells. (1 Ref)

65. CARCINOGENICITY IN RATS OF THE MUTAGENIC COMPOUNDS 1-NITROPYRENE AND 3-NITROFLUORANTHENE.

Ohgaki H, Matsukura N, Morino K, Kawachi T, Sugimura T, Morita K, Tokiwa H, Hirota T
Biochemistry Div., National Cancer Center Res. Inst., Tsukiji 5-1-1, Chuo-Ku, Tokyo 104, Japan
Cancer Lett; 15(1):1-7 1982

Carcinogenicities of 1-nitropyrene (NP) and 3-nitrofluoranthene (NFA) induced in male F344/DuCrj rats by sc injections were studied. NP and NFA are present in diesel exhaust, in pollutants in air, and also in some xerographic toners and copies. NP and NFA were each dissolved in dimethyl sulfoxide (DMSO) at a concentration of 10 mg/ml and injected sc into the back of rats. The 8-wk-old rats were divided into groups; Group I (20 rats: 20 mg NP, 2x/wk x 20 wk), Group II (10 rats: 2 mg NFA, 2x/wk x 15 wk) Group III (20 rats: 0.2 ml DMSO, 2x/wk x 20 wk). Tumors induced by NP or NFA were transplanted into the subcutis of the back and the muscle of the right thigh of 4-wk-old male F344/DuCrj rats. Control rats (Group III) had no changes. Inflammatory nodules and ulcers at the injection site (Group I and II) disappeared by approx day 100. First tumors were found on day 162 (Group I) and day 277 (Group II). No tumor was found in Group III. Tumors were induced in 8/17 rats Group I and 4/10 Group II. Some tumors were serially transplantable in the same strain of rats. Histologically, tumors were extraskeletal osteosarcoma (1/8 tumors Group I), malignant fibrous histiocytomas (7/8 tumors Group I), dermatofibrosarcomas (2/4 tumors Group II), and malignant fibrous histiocytomas (2/4 Group II). (18 Refs)

66. T-CELL MITOGENS CAUSE EARLY CHANGES IN CYTOPLASMIC FREE CA2+ AND MEMBRANE POTENTIAL IN LYMPHOCYTES.

Tsien RY, Pozzan T, Rink TJ
Dept. Physiology-Anatomy, Univ. California, Berkeley, CA, 94720
Nature; 295(5844):68-71 1982

Effects of concanavalin A, phytohemagglutinin, mitogenic calcium ionophores (A23187 and ionomycin), and the cocarcinogen 12-O-tetradecanoylphorbol-13-acetate on cytoplasmic Ca++ level and membrane potential in mouse thymocytes and pig node lymphocytes are reported. Ca++ was measured with the use of a fluorescent indicator (quin2) that was loaded into the cytoplasm of intact cells. (35 Refs)

67. BANDING KARYOTYPE ANALYSIS OF ASCITES LINES OF RAT THYMIC LYMPHOMA (MEETING ABSTRACT).

Sofuni T, Hayashi M, Ogiu T, Ishidate M
Division of Mutagenesis, National Institute of Hygienic Sciences, Tokyo, Japan
Proceedings of the Japanese Cancer Association 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

Eight transplantable ascites lines of rat thymic lymphoma induced by 1-propyl-1-nitrosourea, were analyzed karyotypically by trypsin G-banding method. All ascites lines examined, were found to have near diploid chromosome number (41-43) in their stemlines, and were characterized by duplication of chromosome segment, resulting from trisomy, reciprocal translocation or tandem duplication, except for one line. In the exceptional line, no significant deviation from normal chromosome banding pattern was recognized by the G-method. (no Refs)

68. CYTOGENETICS OF MURINE THYMIC LYMPHOMAS INDUCED BY N-METHYL-N-NITROSOUREA: DIFFERENCE IN INCIDENCE OF TRISOMY 15 IN THYMIC LYMPHOMAS INDUCED IN NEONATAL AND ADULT MICE.

Chan FP, Ens B, Frei JV
Dept. Anatomy, Health Sciences Center, Univ. Western Ontario, London, Ontario N6A 5C1, Canada
Cancer Genet Cytogenet; 4(4):337-344 1981

Chromosome complements of murine thymic lymphomas induced by an alkylating agent N-methyl-N-nitrosourea (MNUA) were analyzed microscopically and karyotypically using the Q-banding technique. The chemical carcinogen was injected intraperitoneally into either neonatal or 7-wk-old CFW/D mice. In addition, thymic lymphomas induced in 7-wk-old AKR mice and thymic lymphomas developed spontaneously in this strain were also examined. All six lymphomas induced in neonatal CFW/D had hyperdiploid cell lines that accounted for 90% of the cells analyzed. Chromosome analysis of lymphomas induced in adult CFW/D mice showed that only four out of nine lymphomas had predominantly hyperdiploid cell lines. The remaining five lymphomas had diploid modal chromosome number although they also carried a variant line characterized by 41 chromosomes. All eight lymphomas induced in adult AKR mice and six out of seven spontaneous AKR lymphomas showed predominantly diploid modal line. The remaining spontaneous lymphoma had a hyperdiploid stem l ine of 41 chromosomes. Microscopic and karyotypic analysis further identified trisomy 15 as the regular chromosome abnormality in the hyperdiploid cells in lymphomas of each group, whereas cells with diploid chromosome number had no detectable chromosome abnormality. Additional trisomies were also found, but their appearance was restricted to individual tumors. Thus, the incidence of trisomy 15 in lymphomas induced by MNUA in adult CFW/D and AKR mice, as well as in the spontaneous AKR lymphomas, is significantly lower than that in lymphomas induced in neonatal mice by the same carcinogen. (Author abstract) (19 Refs)

EXPERIMENTAL STUDIES: DNA TUMOR VIRUSES

69. PERSISTENT INFECTION WITH ADENOVIRUS TYPES 5 AND 6 IN LYMPHOID CELLS FROM HUMANS AND WOOLLY MONKEYS.

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Dept. Pediatrics, Yale Univ. Sch. Medicine, 333 Cedar St., New Haven, CT, 06510
J Infect Dis; 145(1):83-88 1982

Chronic infection with adenovirus Types 5 and 6 was established in primary mononuclear leukocytes from human umbilical cord blood and in Epstein-Barr virus (EBV)-transformed B lymphocytes from human umbilical cord blood and from woolly monkey blood. Adenovirus could be recovered from cultures of primary leukocytes and of EBV-transformed lymphocytes for 2 and 3 mo, respectively, without visible alteration of cell growth. Infection in cultures of EBV-transformed lymphocytes from woolly monkey blood was obliterated by exposure to antibody, but EBV-transformed lymphocytes from human umbilical cord blood contained small amounts of virus for prolonged periods that restored infection in the culture when antibody was removed. Thus, chronic infection of lymphoid cells by some adenoviruses is maintained by at least two mechanisms: cell-to-cell spread of virus in the absence of antibody and intracellular persistence of infectious virus in the presence of antibody. (Author abstract) (18 Refs)

70. ALTERED PROPERTIES OF TUMORS INDUCED BY ADENOVIRUS TYPE 12 DNA FRAGMENT TRANSFORMED CELLS AFTER GROWTH IN IMMUNOCOMPETENT RATS.

Moriuchi T, Yamashita T, Imamura M, Fujinaga K
Dept. Molecular Biology, Cancer Res. Inst., Sapporo Medical Coll., S-1, W-17, Chuo-ku, Sapporo 060, Japan
Int J Cancer; 29(1):101-105 1982

The GY1-3-1 cell line, which was derived from a rat cell line transformed by the Ad 12 HindIII-G fragment, can induce tumors in newborn rats, but not in mature rats. However, when 10 mature rats were transplanted with a large number of GY1-3-1 tumor fragments, two developed tumors with a long latency period. These two tumors (GY1-3M and GY1-3Y) were quite different in properties from the originally inoculated GY1-3-1 tumor. Tumor transplantation studies revealed that both GY1-3M and GY1-3Y tumors could grow in mature rats, and the number of takes with transplanted tumor was 100% with GY1-3M tumor and 40% with GY1-3Y tumor. Histopathologically original GY1-3-1 tumor showed a morphology of undifferentiated sarcoma, while the histologic picture of GY1-3M and GY1-3Y tumors was similar to that encountered in human fibrosarcoma and malignant fiorous histiocytoma, respectively. Both GY1-3M and GY1-3-1 tumors, when recultured in vitro, gave rise to cell lines with a fibroblastic appearance, although the original GY1-3-1 cell line ex-

hibited an epithelioid morphology. In chromosome analysis, the GY1-3-1 cell line was pseudodiploid, while the cell lines from GY1-3M and GY1-3Y tumors were hyperdiploid or near-triploid. The metacentric marker chromosome, M1, was present in mitotic cells of the GY1-3-1 line and of the GY1-3M tumor lines, but absent from the GY1-3Y tumor lines. By Southern blot hybridization, multiple bands of cellular DNAs from parental GY1-3-1 cells hybridized with labeled Ad12 HindIII-G, while only a single band hybridized in DNAs from both GY1-3M and GY1-3Y tumors. (Author abstract) (15 Refs)

71. PROPERTY OF MOUSE ENDOGENOUS C TYPE VIRUS ACTIVATED BY ADENOVIRUS CARCINOGENESIS (MEETING ABSTRACT).

Ohmori M, Kobayashi S, Ogawa K

Department of Pathology, Okayama University Medical School, Okayama, Japan

Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

Endogenous C type virus of C3Hf mice is activated by adenovirus carcinogenesis and this virus induces lymphoma. The density of purified C particles is 1.15-1.18 by RbCl density gradient analysis, and has the antigen common to leukemia viruses Gross-MuLV, Molony-MuLV, Rauscher-MuLV P30, AKR-LV P30, and FeLV P27 by immunodiffusion reaction. Its structural proteins, P30, is the main band, and P70, P59, P43, P15 and smaller ones reveal minor bands by sodium dodecyl sulphate-polyacrylamide gel electrophoresis. From these results it is assumed that this virus has a property different from known oncorna viruses. (no Refs)

72. NEW EPSTEIN-BARR VIRUS VARIANTS FROM CELLULAR SUBCLONES OF P3J-HR-1 BURKITT LYMPHOMA.

Heston L, Rabson M, Brown N, Miller G

(c/o Miller) Dept. Epidemiology and Public Health, Yale Univ. Sch. Medicine, New Haven, CT, 06510

Nature; 295(5845):160-163 1982

Correlation between biological properties and genome structure was examined in 29 subclones of HR-1 virus, an Epstein-Barr virus (EBV) mutant that does not immortalize lymphocytes or induce lymphomas. None of the 29 clones spontaneously released EBV DNA in an amount comparable to that of the parental line. Differences in viral DNA content correlated with lower levels of viral capsid antigen (VCA) clones. Enhanced VCA expression occurred in five clones that released large amounts of DNA after treatment with 12-O-tetradecanoylphorbol-13-acetate (TPA). The subclonal viruses resembled HR-1 in lack of immortalization, cytotoxicity, and interference with transformation; unlike HR-1, they did not induce virus early antigen (EA) synthesis in Raji cells. Differences in the DNAs of nontransforming virus (HR-1 and its subclones) and two transforming EBV strains were found to involve at least six regions of the genome. HR-1 DNA differed from the DNA of cloned and transforming viruses in that it contained three or four size variants of EcoRI ABC het fragments. Possible involvement of the fragments in EA induction is noted. (22 Refs)

73. ESTABLISHMENT OF B-LYMPHOBLASTOID CELL LINES FROM MAREK'S DISEASE VIRUS-INDUCED TUMORS IN TURKEYS.

Nazerian K, Elmubarak A, Sharma JM

Regional Poultry Res. Lab., U. S. Dept. Agriculture, 3606 East Mount Hope Road, East Lansing, MI, 48823

Int J Cancer; 29(1):63-68 1982

Four lymphoblastoid cell lines were established from tumors of turkeys inoculated with high doses of the GA strain of Marek's disease virus (MDV). Unlike other MD lymphoblastoid cell lines of chicken origin, these MDV transformed turkey lines appear to be B lymphocytes and produce immunoglobulin. Growth characteristics of these cell lines are slightly different; however, they all produce low levels of MDV-specific antigen and carry the complete genome of the virus as determined by virus rescue in the chicken or in duck embryo fibroblast cultures. These cell lines are pathogenic for chickens and produce virus-induced MD lesions. All four lines are free of the herpesvirus of turkeys, reticuloendotheliosis virus, and three lines are also free of avian leukosis virus. They all have typical normal turkey chromosomes and are positive for Marek's disease tumor-associated surface antigen. (Author abstract) (24 Refs)

EXPERIMENTAL STUDIES: RNA TUMOR VIRUSES

74. INCREASED RESPONSES TO LYMPHOKINES ARE CORRELATED WITH PRELEUKEMIA IN MICE INOCULATED WITH MOLONEY LEUKEMIA VIRUS.

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Biological Carcinogenesis Program, NCI-Frederick Cancer Res. Facility, Frederick, MD, 21701

Proc Natl Acad Sci USA; 78(12):7712-7716 1981

In various mouse strains, inoculation with Moloney leukemia virus results in the establishment of an acute viremia which in most cases is followed by the induction of leukemia. Also associated with the viremia is the development of a chronic cellular immune response detectable in vitro by the ability of viral proteins to induce splenic lymphocyte proliferation. Previous studies have demonstrated that, in the absence of this cellular immune response, leukemia does not develop irrespective of whether viremia is present. In vitro proliferative responses to antigens involve the nonspecific response of various subpopulations of lymphocytes to lymphokines produced by antigen-specific Thy 1+, Lyt 1+,2-lymphocytes. The studies presented here concern the effects of a chronic immune response in viremic mice on the frequency of lymphocytes capable of responding to lymphokines in vitro. The data demonstrate that the number of responsive lymphocytes is increased 30-to 100-fold in preleukemic mice and that such increases are dependent upon the induction of an immune response in viremic mice. The role of this altered immune response in leukemia is discussed. (Author abstract) (18 Refs)

75. LYSOZYME IN SCHWARTZ AND MOLONEY VIRUS-INDUCED LYMPHOBLASTIC LEUKAEMIA.

Chatterjee G, Das S, Basu A, Mitra S
Chittaranjan Natl. Cancer Res. Center, 37, S.P. Mookerjee Road, Calcutta - 700 026, India
Gan; 72(6):906-909 1981

Studies have been made on lysozyme in serum and tissue homogenates in normal and leukemic mice. An increase in serum lysozyme level occurred in mice bearing both strains of leukemia as compared to the normal counterparts. Moreover, the elevated enzyme levels seem to be related to the rise in neutrophils in peripheral blood. In the spleen and kidney of leukemic mice, the lysozyme level was found to be lower than in the normals, while the enzyme level remained more or less unaltered in the liver. The findings are discussed in relation to other reports in the literature. (Author abstract) (21 Refs)

76. EXPRESSION OF THY1, TL AND LYT ANTIGENS ON SPONTANEOUS LEUKEMIAS OF BALB/MO STRAIN OF MICE.

Strzadala L, Opolski A, Kisielow P
Dept. Tumor Immunology, Inst. Immunology and Experimental Therapy, Czerska 12, 53-114 Wroclaw, Poland
Arch Immunol Ther Exp (Warsz); 29(4):439-441 1981

The expression of Thy1, and Lyt antigens on spontaneous BALB/Mo leukemias has been studied. The results obtained thus far indicate that a majority of leukemias express TL antigen and differentiated Lyt phenotype. This observation and other findings demonstrating and existence of TL+ thymocytes with different Lyt phenotypes in normal thymus of young mice lends support for the hypothesis that TL+Lyt2+ phenotype defines this stage in the T cell differentiation pathway, which is particularly sensitive to leukemic transformation. (Author abstract) (6 Refs)

77. BEHAVIOUR OF GROSS - VIRUS LEUKAEMIA IN PARABIOTIC MICE (MEETING ABSTRACT).

Tatar Kiss Z, Ember I, Kertai P
University Medical School, Debrecen, Hungary
Ninth Congress of the Haematological Society, October 1-3, 1981, Debrecen, Hungary. The Society 175 pp., 1981.

According to literary data leukemic cells transplanted into Wc/F rats cause cellular and humoral immune reactions, the latter being responsible for the regression of leukemia. For further evidence C3H x AKR/F1 hybrids (susceptible for fatal leukemia) and spontaneously healing C3H mice were conjugated in parabiosis. Five days later 1 x 10(6) leukemic cells were injected into F1 hybrid partners. Although duration of survival was longer than that of non-parabiotic animals, each of them perished in the end. However, pretreated and healed C3H partners completely protected hybrids from leukemia. Even grafting of tumor cells after separation remained ineffective. These experiments seem to prove the role of delayed humoral factors. (no Refs)

78. INVESTIGATION OF HEXOKINASE, FRUCTOKINASE AND PHOSPHOFRUCTOKINASE IN LYMPH NODES OF MICE WITH GROSS-VIRUS LEUKAEMIA (MEETING ABSTRACT).

Arany I, Rady P, Kertai P
University Medical School, Debrecen, Hungary
Ninth Congress of the Haematological Society, October 1-3, 1981, Debrecen, Hungary. The Society 175 pp., 1981.

Hexokinase, phosphofructokinase and pyruvatkinase have great significance in the regulation of glycolysis. The extreme glycolysis of tumorous cells is the result of alteration of these enzymes, caused by deviation of enzyme-synthesis or isoenzyme-structure. Based on investigations of lymph nodes of mice with Gross-virus leukemia, the following conclusions were made: 1) In lymphatic leukemia decreased activity of hexokinase can be observed because of alteration of the subcellular distribution of the enzyme. Hexokinase bound to mitochondria plays an active role in stimulating respiration of leukemic lymphocytes. 2) The activity of phosphofructokinase increases in the cytosol, while its cytrate-sensibility decreases thus increasing glycolysis of leukemic cells. 3) The activity of pyruvatkinase also increases in leukemia. Kinetic investigations show that pyruvatkinase is present in leukemic cells in an interconvertible form, which together with phosphofructokinase helps the enhanced glycolysis. (no Refs)

79. QUANTITATIVE VARIATIONS IN THE EXPRESSION OF H-2 ANTIGENS ON MURINE LEUKEMIA VIRUS-INDUCED TUMOR CELLS CAN AFFECT THE H-2-RESTRICTION PATTERNS OF TUMOR-SPECIFIC CYTOLYTIC T LYMPHOCYTES.

Plata F, Tilkin AF, Levy JP, Lilly F
Unite d'Immuno-Parasitologie, Institut Pasteur, 25 rue du Docteur Roux, 75015 Paris, France
J Exp Med; 154(6):1795-1810 1981

Expression of major histocompatibility antigens (H-2) Kd and Dd was quantified in three different leukemia cell lines induced by Gross murine leukemia virus (MuLV) in BALB/c (H-2d) mice. Preferential recognition of Gross MuLV-induced tumor antigen with H-2Kk or H-2Dd antigen by tumor-specific cytotoxic T lymphocytes (CTL) from BALB/c mice was correlated with the quantitations. The three BALB/c tumor lines differed in amount of H-2Kd and H-2Dd antigens expressed on the cell surface; the variations were reflected in quality as target cells to Gross MuLV-specific CTL from BALB/c mice. The results indicated that restriction of tumor-specific CTL activity by H-2 can be directed at the target cell level by the quantitative modulation of H-2K or H-2D antigen expression; separate tumors induced by the same MuLV in the same or in H -2-congeneic strains of mice may vary in absolute amount of H-2K or H-2D antigen expressed on the cell surface. (35 Refs)

80. DIFFERENTIAL REGULATION OF H-2 ANTIGEN EXPRESSION IN TUMORS AND ITS BIOLOGIC CONSEQUENCES.

Schmidt W, Alonso A, Leben L, Festenstein H, Martin WJ, Meruelo D, Schirrmacher V, Rajan, Lennox ES, Bach FH, Rogers MJ
Dept. Virology FB23, Justus-Liebig-Univ., D-6300 Giessen, W. Germany
Transplant Proc; 13(4):1814-1818 1981

Variations in H-2 antigen expression and their effects on immune response in 10 mouse leukemia cell lines were studied. Cell lines were derived from spontaneous leukemias in AKR mice and AKR/Gross murine leukemia virus (MuLV)-induced leukemias in BALB.K(H-2k) mice, and were designated K36.16, k-GV, 110, 344, 389, 424, 339, 365, 369, and 422. Assays of complement-dependent cytotoxicity indicated that expression of both H-2Kk and H-2dk antigens was slightly increased in 365 and highly increased in 339 and 369. Expression of H-2.Kk antigen was reduced and expression of H-2Dk was normal in 110 and 424. Expression of H-2Kk was absent, and expression of H-2Dk was normal or reduced in K36.16, k-GV, 334, 389, and 422. Loss of H-2Kk, when observed, was consistent within cell lines in vivo and in vitro. Results of cytotoxi-

city assays were confirmed by similar results with absorption and immunofluorescence assays. Labeling experiments with [3H]- or [14C]-arginine indicated that differences in H-2Kk and H-2Dk expression are reflected at the level of biosynthesis and are not due to turnover or blocking at the cell surface. Results of stimulation of cytotoxic effector cells (CTL) with k-GV or 369 tumor cells showed that cytolysis of cells lacking H-2Kk is low; H-2Kk is apparently important for H-2-restricted cytolysis of cells by CTL sensitized against viral antigens. Changes in H-2Kk expression may play an important role in the development of leukemia. (12 Refs)

81. STRUCTURE OF RETROVIRAL RNAS PRODUCED BY CELL LINES DERIVED FROM SPONTANEOUS LYMPHOMAS OF AKR MICE.

Pedersen FS, Crowther RL, Hays EF, Nowinski RC, Haseltine WA
Dept. Molecular Biology, Univ. Aarhus, DK-8000 Aarhus C, Denmark
J Virol; 41(1):18-29 1982

The retrovirus expression of eight independent lymphoid cell lines derived from spontaneous thymomas of AKR mice was investigated. The RNase T1 finger-prints of viral 70S RNA produced by these cell lines were compared with genome structures of the non-leukemogenic Akv virus and with two types of cloned leukemogenic viruses derived from one of the thymoma cell lines. Viral RNAs from three cell lines, SL3, 4, and 7, were indistinguishable from one another. The fingerprint patterns indicated that these cell lines produce equal amounts of two prototype, leukemogenic SL viruses that were previously isolated from the SL3 cell line. Viral RNA produced by the SL1 and SL2 cell lines contained similar components, but at a different ratio. Two other cell lines (SL5 and SL11) produced viral RNAs that resemble those of AKR mink cell focus-forming viruses. One additional line, SL9, produced viral RNA of a novel structure. The complex pattern of viral RNA expression observed for these lymphoid cell lines can be interpreted in terms of recombination among three types of endogenous viral sequences: the Akv virus, a xenotropic virus, and an SL (for spontaneous leukemia) virus. (Author abstract) (25 Refs)

82. PATHOGENESIS OF PARALYSIS AND LYMPHOMA ASSOCIATED WITH A WILD MOUSE RETROVIRUS INFECTION: PART 1. AGE- AND DOSE-RELATED EFFECTS IN SUSCEPTIBLE LABORATORY MICE.

Hoffman PM, Ruscetti SK, Morse HC
Neurology Res. (151), Veterans Admin. Medical Center, Charleston, SC, 29403
J Neuroimmunol; 1(3):275-285 1981

The effects of age at time of inoculation and dose of virus on the incidence, latent period, and mortality from paralytic disease and lymphoma were determined in random-bred NIH Swiss and inbred NFS/N mice inoculated with a cloned neurotropic wild-mouse ecotropic murine retrovirus (Cas-Br-M). Paralytic disease, lymphoma, and mortality all exhibited reduced incidence with increasing age at the time of inoculation of NIH Swiss mice with virus (4,000 pock forming units [pfu]/animal ip). NIH Swiss mice inoculated at day 0 with different doses of virus (100-4,000 pfu/animal) exhibited greater incidence and more rapid onset of paralysis. With increasing concentration of virus, earlier death but lower incidence of lymphoma were found. Anti-Cas-Br-M titer was elevated in mice inoculated at age 10 days, but not in paralyzed mice inoculated on days 0-2. Viral protein levels in spleen and brain of Cas-Br-M-infected mice were assayed. Paralysis and lymphoma are independently expressed following inoculation. The results suggest that the different disease manifestation developing after Cas-Br-M inoculation ar caused by virus-host interactions. (16 Refs)

83. EXPRESSION OF MOUSE MAMMARY TUMOR VIRUS (MUMTV) GENES IN LEUKEMIA CELL LINES FROM DBA/2 MICE (MEETING ABSTRACT).

Murakami A, Tanaka H
Institute of Virus Research, Kyoto University, Kyoto, Japan
Proceedings of the Japanese Cancer Association, 40th Annual Meeting, October 1981, Sapporo, Japan. The Association 415 pp., 1981.

We investigated the expression of MuMTV genes at the RNA level in lymphoid cells, the proposed intermediate carriers of milk-borne MuMTV. Six lymphoid cell lines were established from spontaneous DBA/2 mouse leukemias, some of which were known to contain MuMTV pronucleocapsids. MuMTV RNA was measured by molecular hybridization using cyclic DNA synthesized in exogenous reaction with MuMTV (C3H) RNA as a template. More than 0.005% of cellular RNA was MuMTV-specific. These results are discussed with those with normal lymphoid tissues and mammary gland epithelia. (no Refs)

84. PROGRAMMED AND ALEATORY ELEMENTS IN THYMIC LEUKEMIA.

Tempelis LD, Zielinski CC, Waksal SD, Khiroya RH, Schwartz RS, Martin WJ, Bach FH, Alexander
Winter Res. Lab., Mount Sinai Medical Center, Milwaukie, WI, 53201
Transplant Proc; 13(4):1854-1857 1981

A study was undertaken to test whether thymocytes that possess receptors for the viral envelope glycoprotein gp70 of a given thymotropic leukemogenic virus are the target cells for leukemogenic transformation by that particular virus. Thymocytes derived from control mice showed a consistently similar pattern: a high expression of Thy-1.2, Lyt-1, and Lyt-2, and a low expression of H-2Kk and Iak. Receptors for peanut agglutinin were uniformly present in high percentages. Moloney virus (MuLV) antigen expression was low on thymocytes derived from control mice. Each tumor had a distinctive phenotype. All phenotypes were positive for Thy-1.2 and MuLV antigen. The thymocytes from thymomas induced by each cloned polytropic retrovirus (PTV) presented uniformly with a stable phenotype characteristic of that particular PTV clone. The percentage of MuLV-expressing thymocytes was high. Thymocytes from CBA and HRS mice 4, 6, and 12 wk after injection with PTV 1 and PTV 2 were analyzed for an immediate effect on the thymocyte phenotype. The phenotype of thymocytes derived from these mice was not changed drastically compared to uninjected control mice. Results indicate that the surface phenotype of thymocytes from spontaneously occurring thymomas is random. (9 Refs)

85. CELLULAR ORIGIN AND ROLE OF MINK CELL FOCUS-FORMING VIRUSES IN MURINE THYMIC LYMPHOMAS.

Chattopadhyay SK, Cloyd MW, Linemeyer DL, Lander MR, Rands E, Lowy DR
NIH, Building 41, Room A114, Bethesda, MD, 20205
Nature; 295(5844):25-31 1982

Embryo DNA of AKR mice contains several copies of intact mink cell focus-forming (MCF)-like env gene sequences with a proviral structure. In spontaneous thymic tumors, these MCF-like env sequences have regularly recombined with a specific region of the 3' end of ecotropic env. This specific re-

combination is probably a critical event in the pathogenesis of spontaneous AKR tumors. (Author abstract) (52 Refs)

86. ANTIGEN-SPECIFIC MURINE T-CELL LYMPHOMAS: FUNCTIONAL HETEROGENICITY.

Azar Y, Eidelsztein P, Yefenof E, Chriqui E, Katz-Gross A, Kedar E, Ben-Sasson SZ
Lautenberg Center for General and Tumor Immunology, Hebrew Univ.-Hadassah Medical Sch., P.O. Box 1172, Jerusalem 91010, Israel
Cell Immunol; 65(1):194-200 1981

Two ovalbumin (OVA)-specific helper lymphomas (designated ROT/6.1 and ROT/6.2) were established by transformation of enriched, OVA-immune T cells with the radiation leukemia virus (RadLV). Shortly after establishment these lymphomas provided carrier (OVA)-specific help for anti-hapten antibody response. However, 5 mo later ROT/6.1 lost its OVA specificity and could augment anti-hapten antibody response in the presence of an unrelated carrier. ROT/6.2 retained its antigen-specific helper function over 10 mo of repeated passaging. This OVA-specific helper line inhibited anti-hapten antibody response when given together with an unrelated carrier. Cloning of ROT/6.2 by limiting dilution revealed that only 3 of 10 clones tested had OVA-specific helper activity. None of the clones could induce antigen-specific DTH reaction. The interrelationship between the functional heterogenicity, specificity, and stability of the helper lines is discussed. (Author abstract) (17 Refs)

87. MULTIPLE ARRANGEMENTS OF VIRAL DNA AND AN ACTIVATED HOST ONCOGENE IN BURSAL LYMPHOMAS.

Payne GS, Bishop JM, Varmus HE
Dept. Biochchemistry and Biophysics, Univ. California, San Francisco, CA, 94143
Nature; 295(5846):209-214 1982

Proviruses of avian leukosis virus (ALV) are located in the vicinity of a putative cellular oncogene (c-myc) in ALV-induced bursal lymphomas. Enhanced expression of c-myc occurs in association with proviruses found in any of three configurations: (I) on the 5' side ('upstream') of c-myc in the same transcriptional orientation; (II) on the 3' side '(downstream') of c-myc in the same orientation; (III) upstream, in the transcriptional orientation opposite to that of c-myc. Thus, activation of adjacent cellular genes by retroviral DNA can involve mechanisms other than provision of a transcriptional promoter. (Author abstract) (38 Refs)

88. CHARACTERIZATION OF A BONE MARROW CELL LINE TRANSFORMED BY ABELSON'S MURINE LEUKEMIA VIRUS.

Pinter A, Borzsonyi M
Orszagos Kozegeszsegugyi Intezet, Budapest, Hungary
Magy Onkol; 25(4):217-226 1981

Development of transformed cell line (Gr 17) was observed after infection of a long-term bone marrow cell culture from BALB/c mice with Abelson's murine leukemia virus (strain P 160) (A-MuLV). According to their phenotype, the Gr 17 cells corresponded to the early maturation form of B lymphoid cells (pre-B lymphoblasts). The results of the tests for alpha-naphthylacetate esterase, Hb, phagocytosis, and membrane surface Ig were negative, but cytoplasmic IgM was found. In contrast to the hitherto described cell lines obtained by transformation with A-MuLV, hypodiploid chromosome set and the presence of metacentric chromosome due to translocation were observed. Development of thymus-independent generalized lymphoma was observed after transplantation of Gr 17 cells (2 x 10(7) cells iv) in 4-6-wk-old male and female BALB/c mice. The take rates were 9/10 in the females and 8/10 in the males. The mean latent periods were 41 days in the females and 50 days in the males. Typical Abelson's tumors were induced by the virus produced by the cell line in newborn BALB/c mice. (27 Refs) (In HUN)

89. LONG TERMINAL REPEAT OF MURINE RETROVIRAL DNAS: SEQUENCE ANALYSIS, HOST-PROVIRAL JUNCTIONS, AND PREINTEGRATION SITE.

Van Beveren C, Rands E, Chattopadhyay SK, Lowy DR, Verma IM (c/o Verma) Tumor Virology Lab., Salk Inst., San Diego, CA, 92138
J Virol; 41(2):542-556 1982

The nucleotide sequence of the long terminal repeat (LTR) of three murine retroviral DNAs has been determined. The data indicate that the U5 region (sequences originating from the 5' end of the genome) of various LTRs is more conserved than the U3 region (sequences from the 3' end of the genome). The location and sequence of the control elements such as the 5' cap, 'TATA-like' sequences, 'CCAAT-box,' and presumptive polyadenylic acid addition signal AATAAA in the various LTRs are nearly identical. Some murine retroviral DNAs contain a duplication of sequences within the LTR ranging in size from 58 to 100 base pairs. A variant of molecularly cloned Moloney murine sarcoma virus DNA in which one of the two LTRs integrated into the viral DNA was also analyzed. A four-base-pair duplication was generated at the site of integration of LTR in the viral DNA. The host-viral junction of two molecularly cloned AKR-murine leukemia virus DNAs (clones 623 and 614) was determined. In the case of AKR-623 DNA, a three- or four-base-pair direct repeat of cellular sequences flanking the viral DNA was observed. However, AKR-614 DNA contained a five-base-pair repeat of cellular sequences. The nucleotide sequence of the preintegration site of AKR-623 DNA revealed that the cellular sequences duplicated during integration are present only once. Finally, a striking homology between the sequences flanking the preintegration site and viral LTRs was observed. (Author abstract) (44 Refs)

90. CHARACTERIZATION OF RETICULOENDOTHELIOSIS VIRUS STRAIN T DNA AND ISOLATION OF A NOVEL VARIANT OF RETICULOENDOTHELIOSIS VIRUS STRAIN T BY MOLECULAR CLONING.

Chen IS, Mak TW, O'Rear JJ, Temin HM
McArdle Lab. Cancer Res., Univ. Wisconsin, Madison, WI, 53706
J Virol; 40(3):800-811 1981

Reticuloendotheliosis virus strain T (REV-T) is a highly oncogenic avian retrovirus which causes a rapid neoplastic disease of the lymphoreticular system. Upon infection, this virus gives rise to two species of unintegrated linear viral DNA, which are 8.3 and 5.5 kilobase pairs long and represent the helper virus (REV-A) and the oncogenic component (REV-T), respectively. Restriction endonuclease cleavage maps of these two DNA components indicate that REV-T DNA has a large portion of the genome deleted with respect to REV-A DNA and a substitution about 0.8 to 1.5 kilobase pairs long that is unrelated to REV-A DNA. These additional sequences comprise the putative transforming region of REV-T (rel). A chicken spleen cell line transformed by REV-T produced virus which upon infection gives rise to three species of unintegrated

linear viral DNA (8.3, 5.5, and 3.3 kilobase pairs). We isolated the proviruses of the 8.3-and 3.3-kilobase pair species from this cell line by cloning in the phage vector Charon 4A. Restriction enzyme mapping showed that the two proviral clones are proviruses of REV-A and a variant of REV-T, respectively. A subclone of the variant REV-T provirus specific for the rel sequences of REV-T was used as a hybridization probe to demonstrate that the rel sequences are different from the putative transforming sequences of Schmidt-Ruppin Rous sarcoma virus strain A, avian myelocytomatosis virus, avian myeloblastosis virus, avian erythroblastosis virus, Abelson murine leukemia virus, and Friend erythroleukemia virus. In addition, the rel-specific hybridization probe was used to identify a specific set of sequences which are present in uninfected avian DNAs digested with several restriction enzymes. The corresponding cell sequences are not arranged like rel in REV-T. (Author abstract) (46 Refs)

91. THE U3 PORTION OF FELINE LEUKEMIA VIRUS DNA IDENTIFIES HORIZONTALLY ACQUIRED PROVIRUSES IN LEUKEMIC CATS.

Casey JW, Roach A, Mullins JI, Burck KB, Nicolson MO, Gardner MB, Davidson N
(c/o Davidson) Dept. Chemistry, California Inst. Technology, Pasadena, CA, 91125
Proc Natl Acad Sci USA; 78(12):7778-7782 1981

The presence and location of DNA sequences related to the U3 and U5 portions of the infectious exogenous feline leukemia virus (FeLV) long terminal repeat (LTR) in various cat DNAs have been determined by hybridization experiments. In uninfected cat DNAs, the U5 LTR segment from the Gardner-Arnstein strain B virus is present at approx 150 copies per cell. This level is approx 10-fold greater than that of endogenous internal FeLV sequences. The U5 sequences differ in copy number and, to some extent, in location from one animal to another. For any one animal, the sequence organization of the U5 segments is the same among different tissues, showing that the pattern is inherited through the germ line. Most importantly, the viral U3 LTR probe hybridizes only very weakly with uninfected cat DNAs. Both the U3 and the U5 regions of the LTR from the Gardner-Arnstein strain of virus cross-hybridize with DNA derived from four other infectious FeLVs representing A, B, and C subtypes. Thus, the U3 region may be used as a probe for studying the number and location of exogenously acquired FeLV proviruses in infected cat tissues. In some cases exogenously acquired proviruses are present in unique sites in the genome of virus-positive cat lymphosarcomas, indicating a monoclonal origin for the tumor. In other tumors, the proviral sequences are ran domly distributed over many sites. Lymphosarcomas of virus-negative cats have no exogenous U3 sequences despite epidemiological evidence of an association of virus-negative leukemia with exposure to FeLV. (Author abstract) (17 Refs)

92. EXPRESSION OF BOVINE LEUKEMIA VIRUS GENOME IS BLOCKED BY A NONIMMUNOGLOBULIN PROTEIN IN PLASMA FROM INFECTED CATTLE.

Gupta P, Ferrer JF
Cooperative Leukemia Studies Unit, Sch. Veterinary Medicine, Univ. Pennsylvania, Kennett Square, PA, 19348
Science; 215(4531):405-407 1982

Plasma of cattle infected with bovine leukemia virus contains a soluble factor that blocks the expression of the viral genome in cultured lymphocytes. The blocking factor is not present in plasma of bovine leukemia virus-free cattle or of cattle infected with common bovine viruses. Blocking of bovine leukemia virus expression by the plasma factor is reversible, and seems to be mediated by a nonimmunoglobulin protein molecule. (Author abstract) (13 Refs)

REVIEWS AND OTHER RELATED STUDIES

93. SUMMARY OF THE SYMPOSIUM ON ATYPICAL LEUKEMIA.

Hoshino T, Kita Y
Second Dept. Internal Medicine, Kyoto Univ., Kyoto, Japan
Rinsho Ketsueki; 22(6):827-831 1981

Atypical leukemia (ATL) was discussed with respect to unique pathological patterns, foci of pathological analysis, and treatment. ATL was differentiated from overt acute leukemia and was defined to include hypoplastic leukemia (HL) and smouldering acute leukemia (SAL). Incidence of ATL was observed to be increasing in the general population of Japan as the elderly segment of the population increases, thus differences between HL in the elderly and HL in the young were thought to be important. Some researchers thought that leukemia occurring in the elderly patients should be considered to be atypical anemia, and that this should be taken into account when combination chemotherapy was initiated. Blood cell turnover, hyperplasia of stem cells, and the hemopoietic environment were the foci of pathological analysis of ATL. Appropriateness of mild or intensive chemotherapeutic treatment of ATL was discussed. Proponents of intensive chemotherapy thought that intensive chemotherapy was appropriate when marrow blast cell ratios progressed to greater than 30% during the normal course of the atypical leukemia. Proponents of mild chemotherapy began treatment with steroid hormones and/or transfusions, and when the cases transformed into overt acute myelogenous leukemia, combination chemotherapy was initiated. Other physicians treated the patients with the aim to prevent the transformation of the ATL into overt acute leukemia and to prolong patient survival time renouncing to the goal of inducing complete remission. (no Refs) (In JPN)

94. PRELEUKEMIA AND LEUKEMIA.

Dreyfus B
Unite de Recherches sur les Anemies, INSERM, Hopital Henri Mondor, F-94010 Crete il, France
Blood Cells; 7(3):591-592 1981

The evolution of hemopoietic dysplasia to acute myelogenous leukemia (AML), representing a clinical model of the transformation of cells from benign to malignant state, is reviewed. The failure of myeloblasts and promyelocytes to mature is a major characteristic of cells in typical AML. Clinical observations show reversibility of the maturation arrest and support the notion made on the basis of culture and animal experiments that the leukemic process can be normalized. (10 Refs)

95. AN EPIDEMIOLOGICAL BASIS FOR CANCER CONTROL.

Armstrong B
NH and MRC Res. Unit in Epidemiology and Preventive Medicine, Univ. Western Australia, Dept. Medicine, Nedlands, Australia
Cancer Forum; 5(3):136-143 1981

Primary and secondary prevention of cancer, particularly cancer of the lung, breast, and colon and melanoma, which together account for greater than 40% of new cancer cases and premature mortality is discussed. Primary prevention aims at preventing cancer from occuring by ending exposure to the causal agent either by environmental or life type control. Lung cancer is attributable mainly to cigarette smoking; some cases result from occupational exposure. Breast cancer is associated with nulliparity, first full-term pregnancy at a comparatively late age, low parity, diet, radiation, post-menopausal estrogens, and oral contraceptives. Colon and rectal cancer are mainly related to dietary fiber deficiency and excess fat and meat consumption. Melanoma of the skin is due to exposure to UV radiation. Etiologies of other neoplasms are discussed: brain neoplasms (phenobarbitone use), prostate cancer (diet, cadmium exposure), stomach cancer (diet), leukemia (x-rays, benzene exposure, antineoplastic agent use), pancreatic cancer (diet, cigarette smoking), bladder cancer (occupational exposure to aromatic amines, cigarette smoking), and cervix cancer (sexual promiscuity). Dietary modification, cessation of smoking, and avoidance of excessive exposure to UV light was recommended. Screening methods involved in the secondary prevention of cancer include cervical cytology, proctosigmoidoscopy, and mammography at regular intervals for certain segments of the population. The choice between primary and secondary prevention of cancer is discussed. (20 Refs)

96. CYTOGENETIC ANALYSIS IN HUMAN BONE MARROW TRANSPLANTATION.

Sparkes RS
Div. Medical Genetics, Dept. Medicine, Univ. California Los Angeles Sch. Medicine, Los Angeles, CA, 90024
Cancer Genet Cytogenet; 4(4):345-352 1981

Chromosome and sex chromatin studies have contributed significantly to the evaluation of human bone marrow transplants. In addition to their use in documenting bone marrow engraftment following transplantation, they have been used to (1) evaluate whether recurrent leukemia occurs in donor or rec ipient cells and whether recovery in aplastic anemia results from growth of host or donor cells, (2) demonstrate the bone marrow origin of pulmonary macrophages and hepatic Kupffer cells, (3) show that bone marrow fibroblasts have an origin different from that of the hematopoietic bone marrow cells, (4) evaluate twin zygosity in preparation for transplantation, and (5) show that the defect in Fanconi's anemia is intracellular. (Author abstract) (32 Refs)

97. ONCOGENESIS BY RNA TUMOR VIRUSES.

Koyama T
Dept. Carcinostasis Res., Tokyo Univ. Medical Res. Inst., 4-6-1 Kindai, Minato-ku, Tokyo 108, Japan
Tanpakushitsu Kakusan Koso; 26(14):2121-2129 1981

The origin of retrovirus transforming genes and their oncogenic mechanisms were discussed with respect to literature data. Existence of oncogenic genes in lymphogenous leukemia virus, sarcoma viruses, and acute leukemia viruses was discussed. Oncogenic mechanisms of sarcoma viruses, acute leukemia viruses, and lymphogenous leukemia viruses were reviewed with the aid of analysis at the nucleic acid or protein levels. Various research showed that oncogenesis by retroviruses was not only due to promoter insertion; changes in the manifestation of the c-oncogenic gene, by introduction of DNA rearrangement methods, were also thought to be possible. (77 Refs) (In JPN)

98. COMMENT: PROGRESS IN THE RESEARCH OF LEUKEMIAS.

Yang C
Inst. of Hematology, Chinese Acad. Medical Sciences, Beijing, People's Republic of China
Zhonghua Neike Zazhi; 20(4):193 1981

Progress in leukemia treatment and research over the past few decades is reviewed. Although much progress has been made in China in the chemotherapy of leukemia using plant drugs (eg indirubin, cephalotaxus alkaloids), progress in basic research in the following areas lags far behind other countries: leukemia virus etiology, leukemia cell characteristics (culture, stem cell pathology, etc), preleukemia, screening and synthesis of antileukemic agents, and monoclonal antibodies in diagnosis and therapy. (no Refs) (In CHI)

99. WHAT'S NEW IN CUTANEOUS ONCOLOGY: 1981.

Hu CH
Dept. Dermatology, Stanford Univ. Sch. Medicine, Stanford, CA
Taiwan I Hsueh Hui Tsa Chih; 80(10):1071-1073 1981

New findings related to epidemiologic and environmental influences, viral carcinogenesis, and hybridoma technology with emphasis on implications of new findings in clinical medicine are reviewed. Areas of cutaneous oncology discussed are Kaposi's sarcoma, Merkel cell tumor, malignant sweat gland tumor, Langerhans' cell tumor, and cutaneous T cell lymphoma. (no Refs)

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As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

CHEMICAL CARCINOGENESIS

1. ETHYLENE OXIDE (ETO): EVIDENCE OF CARCINOGENICITY.
Coene RF
National Inst. for Occupational Safety and Health, Cincinnati, OH
Vet Hum Toxicol; 23(6):439-443 1981

DIETARY FACTORS IN CARCINOGENESIS

2. NUTRITIONAL ASPECTS OF CANCER PREVENTION: AN OVERVIEW.
Silverman J
American Health Foundation, Naylor Dana Inst Disease Prevention, Valhalla, NY, 10595
J Am Vet Med Assoc; 179(12):1404-1409 1981

3. FORMATION OF N-NITROSO COMPOUNDS IN FOODS.
Gray JI
Dept. Food Science and Human Nutrition, Michigan State Univ., East Lansing, MI, 48824
ACS Symp Ser; 174():165-180 1981

EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

4. LYMPHOMAS AND LEUKAEMIAS. PART 2: TROPICAL AMERICA.
Jimenez E
Hospital Nacional de Ninos 'Dr. Carlos Saenz Herrera', Apartado 1654, San Jose, Costa Rica
Clin Haematol; 10(3):894-915 1981

5. LYMPHOMAS AND LEUKAEMIAS. PART 1: TROPICAL AFRICA.
Olweny CL
Uganda Cancer Inst., P.O. Box 3935, Kampala, Uganda
Clin Haematol; 10(3):873-893 1981

6. MALIGNANT MELANOMA.
Creagan ET
Div. Medical Oncology, Mayo Clinic, Rochester, MN, 55905
Compr Ther; 7(12):36-44 1981

7. MELANOTIC TUMORS OF THE UVEA AND RETINA.
Schmitt H
Universitats-Augenklinik, Theodor-Stern-Kai 7, D-6000 Frankfurt am Main, W. Germany
Med Klin; 76(24):672-675 1981
In GER

CELLULAR AND MOLECULAR MECHANISMS IN CARCINOGENESIS

8. THE NATURAL HISTORY OF CARCINOGENESIS: IMPLICATIONS OF EXPERIMENTAL CARCINOGENESIS IN THE GENESIS OF HUMAN CANCER.
Pitot HC, Goldsworthy T, Moran S
McArdle Lab. for Cancer Res., Dept. Oncology, Medical Sch., Univ. Wisconsin, Madison, WI, 53706
J Supramol Struct Cell Biochem; 17(2):133-146 1981

9. CURRENT CONCEPTS AND CONTROVERSIES IN CHEMICAL CARCINOGENESIS.
Weinstein IB
Div. Environmental Sciences, Inst. Cancer Res., Columbia Univ. Coll. Physicians and Surgeons, New York, NY, 10032
J Supramol Struct Cell Biochem; 17(2):99-120 1981

VIRAL AND IMMUNOLOGICAL ASPECTS OF CARCINOGENESIS

10. BURKITT'S LYMPHOMA.
Ambrus JL, Ambrus CM
Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
J Med; 12(6):385-413 1981

11. PRIMARY HEPATIC CARCINOMA.
Iosquin CJ
Catedra de Medicina Interna A, Facultad de Ciencas Medicas, La Plata, Argentina
Rev Fac Cienc Med La Plata; 4(2):27-31 1981
In SPA

METHODOLOGY IN CARCINOGENESIS RESEARCH

12. MUTAGENESIS AND CARCINOGENESIS TESTING IN VITRO.
Casto BC
Northrop Services, Incorporated, P.O. Box 12313, Research Triangle Park, NC, 27709
Biotechnol Bioeng; 23(12):2659-2671 1981

OTHER REVIEWS IN CARCINOGENESIS

13. CANCER IN THE YEAR 2000. A REVIEW.
Saxe[illegible]
Syo[illegible] Syoparekisteri, Liisankatu 21 B, 00170 Helsinki 17, Finland
Duodecim; 97(20):1708-1716 1981
In FIN

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Lymphatic and Hematopoietic Tissues

SERIES CK20 No. 82/07 JULY, 1982

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EPIDEMIOLOGY AND ETIOLOGY OF HUMAN LYMPHORETICULAR MALIGNANCIES: VIRAL STUDIES

1. NATURAL ANTIBODIES TO HUMAN RETROVIRUS HTLV IN A CLUSTER OF JAPANESE PATIENTS WITH ADULT T CELL LEUKEMIA.

Robert-Guroff M, Nakao Y, Notake K, Ito Y, Sliski A, Gallo RC
Dept. Cell Biology, Litton Bionetics, Inc., Kensington, MD, 20895
Science; 215(4535):975-978 1982

Human T cell lymphoma leukemia virus (HTLV) is a human retrovirus (RNA tumor virus) that was originally isolated from a few patients with leukemias or lymphomas involving mature T lymphocytes. Here we report that the serum of Japanese patients with adult T cell leukemia, but not the serum of tested normal donors, contains high titers of antibodies to HTLV. These observations, together with data from Japan showing that adult T cell leukemia is endemic in southwest Japan, suggest that HTLV is involved in a subtype of human T cell malignancy, including Japanese adult T cell leukemia. (Author abstract) (22 Refs)

2. THE AMERICAN BURKITT'S LYMPHOMA REGISTRY: EIGHT YEARS' EXPERIENCE.

Levine PH, Kamaraju LS, Connelly RR, Berard CW, Dorfman RF, Magrath I, Easton JM
Clinical Studies Section, Lab. Viral Carcinogenesis, NCI, Landow Building, Room 1D-12, Bethesda, MD, 20205
Cancer; 49(5):1016-1022 1982

Four hundred twenty-one Americans diagnosed as having Burkitt's lymphoma (BL), 409 from the United States, were studied by the American BL Registry to obtain information about the cause and control of this disease. Of these 421 cases, 256 were confirmed by our pathologists as being morphologically indistinguishable from African BL. A relationship between age and organ involvement was observed; cervical lymph nodes, ileum, and nasopharynx were initial sites of involvement primarily in younger patients. Although the Epstein-Barr virus (EBV) was less frequently associated with American BL than African, a high antibody titer to the EBV capsid antigen was associated with a more favorable prognosis. American BL resembled African BLs time-space clustering, male predominance, and excellent response to chemotherapy. Unlike African BL, however, more patients had involvement of cervical lymph nodes and bone marrow at an early stage of disease. American BL appears to be a more heterogenous disease than African BL. (Author abstract) (28 Refs)

3. AN EBV-ASSOCIATED, SWEDISH CASE OF BURKITT-TYPE MALIGNANT LYMPHOMA.

Biberfeld P, Christensson B, Andersson-Anvret M, Ernberg I, Lewensohn R, Ekman M, Johansson B, Tribukait B
Dept. Pathology, Karolinska Sjukhuset, S-104 01 Stockholm, Sweden
Acta Pathol Microbiol Scand [A]; 89(6):417-424 1981

Morphological, serological, DNA-homology and immunofluorescence studies of a rapidly fatal malignant lymphoma in a 25-yr-old Swedish male revealed most of the characteristics of an EBV-associated Burkitt lymphoma. The various findings are discussed in relation to previously reported observations on endemic (African) and non-endemic Burkitt lymphomas. (Author abstract) (39 Refs)

EPIDEMIOLOGY AND ETIOLOGY OF HUMAN LYMPHORETICULAR MALIGNANCIES: OTHER STUDIES

4. IS APLASTIC ANEMIA A PRE-LEUKEMIC STATE?.

Najean Y, Groupe commun d'etude des aplasies medullaires et des anemies refractaires
Service de Medecine Nucleaire, Hopital Saint-Louis, place du Dr A. Fournier, F 75010 Paris et Unite 204 de l'INSERM, France
Nouv Presse Med; 10(46):3775-3778 1981

Out of 412 adult patients classified as aplastic anemia in a cooperative study group, 22 developed acute leukemia from 3 mo to 5 yr after the initial diagnosis. In 21 of these, retrospective analysis elicited one or several clinical and laboratory data which are uncommon in aplastic anemia but common in preleukemic refractory anemia. Indeed, one half of these patients should have been classified as pre-leukemic, and in the remaining half cell kinetics investigations (analysis of radioactive iron renewal, stem cell cultures and 3H-TdR autoradiography of bone marrow), as well as cytogenetic studies, might have led to a more correct classification. Only one patient, who initially had none of the criteria of pre-leukemic state, responded to androgen treatment with a 4-yr complete remission but died on the 5th yr of acute myeloblastic leukemia. It appears from this retrospective analysis that when all signs of pre-leukemia have been excluded by thorough investigation, aplastic anemia is never, or only exceptionally (1 out of 412 cases), a pre-leukemic condition. (Author abstract) (15 Refs) (In FRE)

5. SMOKING AS RISK FACTOR FOR DIFFERENT FORMS OF CANCER AMONG 26,000 MEN AND WOMEN IN NORWAY. MATCHING OF THE GROUP OF SMOKERS WITH THE CANCER REGISTRY OVER A 12-YEAR PERIOD.

Lund E, Zeiner-Henriksen T
Kreftregisteret, Montebello, Oslo 3, Norway
Tidsskr Nor Laegeforen; 101(34-36):1937-1940 1981

The cancer risk due to smoking was studied among 11,979 men and 13,998 women born between 1895 and 1929 on the basis of data in the Norwegian Cancer Registry for the period 1966-1977. A total of 1,815 cases of cancer were registered for this group during the studied period. Nonsmokers accounted for 22.4% among men and 76.5% among women, ex-smokers for 21.7% and 4.2%, current smokers for 55.4% and 19.1%, and the smoking habits of 0.5% of the men and of 0.2% of the women are unknown. The age-adjusted relative risk (relative to nonsmokers) per 1,000 men was found to be 4.8 for lung cancer and 2.3 for cancer of the urinary bladder and urethra. For women, the relative risk was found to be 1.9 for lung cancer, 1.5 for cancer of the urinary bladder and urethra and 1.3% for cancer of the uterine cervix. The relative risk for all smokers was found to be 1.4 for lip cancer (men), 7.5 for stomach cancer (men), 4.4 for colon cancer (men), 0.9 for larynx cancer, 9.2 (men) and 1.7 (women) for lung cancer, 3.3 for cancer of the uterine cervix, 12.4 for prostate cancer, 3.7 (men) and 1.2 (women) for cancer of the urinary bladder and urethra, 4.8 (men) and 3.4 (women) for lymphoma and leukemia. Significant difference between smokers and nonsmokers was found with respect to laryngeal cancer (men), esophageal cancer (men), cancer of the liver and bile ducts (women) and carcinoma of the uterine cervix as well. The risk of cancer of the upper respiratory passages are higher for pipe smokers than for cigarette smokers, while cigarette smokers had higher risk of

lung cancer than pipe smokers. The cancer risk was found to be lower among ex-smokers than current smokers, and it increased with cigarette consumption. (17 Refs) (In NOR)

6. MORTALITY PATTERNS AMONG WORKERS IN THREE TEXAS OIL REFINERIES.

Thomas TL, Waxweiler RJ, Moure-Eraso R, Itaya S, Fraumeni JF
Occupational Studies Section, Environmental Epidemiology Branch, NCI, Bethesda, MD, 20205
JOM; 24(2):135-141 1982

The cause-specific mortality experience of 2,509 active and retired members of the Oil, Chemical, and Atomic Workers International Union (OCAW) who worked at three oil refineries in the Beaumont/Port Arthur area of Texas was examined to determine whether there might be unusual patterns of fatal disease related to workplace exposures. Deaths that occurred between 1943 and 1979 were identified from membership records of the OCAW headquarters in Denver and from the records of Union locals in Texas which represent workers at the three refineries. Death certificates were obtained from state vital records offices for the decedents. Cause-specific Proportionate Mortality Ratios (PMRs) were calculated using the mortality experience of the US general population as a standard. Excess mortality from stomach cancer occurred among active union members who worked at Refinery A and among active and retired members who worked at Refineries B anc C. PMRs for leukemia, multiple myeloma, and other lymphomas were elevated, especially among retired workers. Relative frequencies of brain tumor deaths were significantly elevated among active members at all three refineries and slightly elevated among retirees at Refineries A and C. Findings suggest that oil refinery workers may have elevated risks of these cancers and indicate that more definitive studies are necessary. (Author abstract) (22 Refs)

7. HYPOTHESIS: THE ENVIRONMENT IS A MAJOR DETERMINANT OF THE IMMUNOLOGICAL SUB-TYPE OF LYMPHOMA AND ACUTE LYMPHOBLASTIC LEUKAEMIA IN CHILDREN.

Ramot B, Magrath I
Dept. Haematology, Chaim Sheba Medical Centre, Tel Aviv Univ. Medical Sch., Tel Aviv, Israel
Br J Haematol; 50(2):183-189 1982

Based on a study of socioeconomic status, the ratio of leukemia to lymphoma, occurrence of their subtypes, acute lymphoblastic leukemia (ALL) in American blacks, and the early age-peak of ALL, a hypothesis is presented that the pattern of lymphoid malignancy in children is dependent on environment and particularly on socioeconomic circumstances. In the most economically underprivileged, ie in equatorial Africans, B-cell lymphomas predominate, leukemia is rare, and ALL may be entirely of the T-cell type. In populations of intermediate economic status, ie in American blacks and Israeli Arabs, B-cell lymphomas are infrequent and the spectrum of lymphoma varies according to the particular local mosaic of environmental and/or genetic factors. In the highest, socially privileged class, ie American whites and Europeans, ALL has a high incidence and is the most common malignant disease in children. (33 Refs)

8. NEOPLASIA AFTER SUCCESSFUL RENAL TRANSPLANTATION.

Disler PB, MacPhail AP, Meyers AM, Myburgh JA
Dept. Medicine, Groote Schuur Hosp., Observatory 7925, Cape Town, South Africa
Nephron; 29(3/4):119-123 1981

A total of 17 confirmed malignancies developed in 14/193 kidney transplant recipients (7.3%), 2-74 mo after the transplant (mean, 32.6 mo). A papillary carcinoma of the thyroid, diagnosed at 2 mo, probably antedated the transplant. Two patients developed squamous cell carcinomas in situ of the cervix uteri; one patient each developed Ph chromosome-positive chronic myelogenous leukemia (this patient died in acute transformation) and Kaposi's sarcoma of the mouth floor. Nine patients developed 10 skin cancers (2 basal and 8 squamous cell carcinomas); 2/9 patients died of disseminated undifferentiated carcinomas of undetermined, possible cutaneous origin. Immunosuppressive therapy was never attenuated to facilitate treatment of the tumor, and transplant function never deteriorated as a result of the tumor or its treatment. All of the cancer patients had received cadaver kidney transplants. As compared to 186 kidney transplant recipients who did not develop cancer (of whom 51 survived greater than 5 yr), the cancer patients showed a higher male:female ratio (3.7:1 vs 1.64:1), a slightly higher mean age at transplantation (41.2 vs 36.0 yr old), a significantly higher prevalence of analgesic nephropathy (5/14 vs 35/186 patients), and significantly fewer treated graft rejection episodes (mean, 0.93 vs 1.71). Both groups were given the same immunosuppressive treatments. Five (62.5%) of the squamous cell carcinomas developed in patients with analgesic nephropathy. The much lower frequency of graft rejection among the cancer patients suggested a generally depressed immune surveillance system in this group. (15 Refs)

9. FAMILIAL ERYTHROLEUKEMIA: FOUR CASES OF THE DIGUGLIELMO SYNDROME IN CLOSE RELATIVES.

Nissenblatt MJ, Bias W, Borgaonkar D, Dixon S, Cody RP
7 Wirt St., New Brunswick, NJ, 08901
Johns Hopkins Med J; 150(1):1-9 1982

Erythroleukemia was diagnosed in three brothers during a 6-mo period in 1976. A son of one leukemic had died 5 yr earlier with erythroleukemia. First-degree relatives of these men were evaluated in an attempt to identify contributing factors. Twenty-four relatives have been studied. Immunoglobulin M was elevated in 14 of 16 persons (mean, 352.8 mg/dl; normal, less than 145 mg/dl; p less than 0.001). This was neither a monoclonal protein nor rheumatoid factor. Age-dependent red cell enzymes were increased. Erythrocyte hexokinase was markedly increased in 23 of 24 persons (mean, 35.05 units/100 ml RBC; normal, less than 18 units; p less than 0.001). Evidence for a hemolytic state was absent. Bone marrow samples in eight first-degree relatives were normal. Cytogenetics were normal in 18 relatives. One leukemic exhibited hypoploidy and a marker chromosome. The association of an immunoglobulin abnormality and enzymopathy in the leukemics and relatives alike suggests a hereditary susceptibility to the development of erythroleukemia. The exact link is not identified. (Author abstract) (35 Refs)

10. LYMPHOMAS AND LEUKEMIAS IN THE RELATIVES OF PATIENTS WITH MYCOSIS FUNGOIDES.

Greene MH, Pinto HA, Kant JA, Siler K, Vonderheid EC, Lamberg SI, Dalager NA
Environmental Epidemiology Branch, NCI, Landow C3-07, Bethesda, MD, 20205
Cancer; 49(4):737-741 1982

Of 526 consecutive patients with cutaneous T-cell lymphomas, 21 had first-degree relatives with lymphoproliferative or hematopoietic malignancies. Twenty-nine such tumors occurred in the 21 kindreds. Hodgkin's disease accounted for one-third of this total, with various leukemias (11 cases), non-Hodgkin's lymphoma (5 cases), and multiple myeloma (3 cases) comprising the remainder. These data suggest that genetically-determined immunoregulatory abnormalities may represent a shared pathway of oncogenesis in diverse lymphoproliferative and hematopoietic malignancies. (Author abstract) (25 Refs)

11. ATAXIA TELANGIECTASIA AND ACUTE LYMPHOBLASTIC LEUKEMIA: REPORT OF A CASE.

Pastore G, Di Montezemolo LC, Madon E
Ospedale Infantile Regina Margherita, Piazza Polonia 94, 10126 Torino, Italia
Tumori; 67(6):585-587 1981

We report a new case of ataxia-telangiectasia (AT) and acute lymphoblastic leukemia (ALL) and review all 21 known cases of AT and ALL. Leukemia in these patients is associated with a male predominance, age older than 10 yr at diagnosis, a white blood cell count higher than 50,000 mm3, and a fatal course. Four patients have been reported who developed T-cell leukemia, three null-cell leukemia and one B-cell leukemia. The AT-ALL patients appear to be at risk for infections related to their immunodeficient status and ALL chemotherapy. In addition, neurologic deterioration has been noted during the early phase of therapy. (Author abstract) (8 Refs)

EPIDEMIOLOGY AND ETIOLOGY OF NON-HUMAN LEUKEMIA AND LYMPHOMA

12. CONTRIBUTION TO EPIDEMIOLOGIC STUDIES OF BOVINE ENZOOTIC LEUKOSIS.

de Alencar RA, Rodrigues FM, Vianna WO
Instituto Biologico, Sao Paulo, Brazil
Biologico; 47(9):249-253 1981

An epidemiologic study of bovine enzootic leukosis (BLV) was performed, using cohabitation (CO), feeding (FE), or blood transfusion (BT). The BT experiment consisted of transferring 200 ml of blood from two serologically positive animals into two that were serologically negative. Immunodiffusion tests (IDT), performed on days 30, 60, 90, 120, and 180, using antigen Leukassay-B, all gave negative results. Eleven cows that were clinically negative for bovine leukemia virus (BLV) showed positive results with the IDT for blood, three showed positive results for colostrum 24 hr after delivery, and five for colostrum 48 hr after delivery. Blood of three of their heifers gave positive results 24 hr after birth and five gave positive results 48 hr after birth; 6 mo later none of the heifers gave positive results. The CO and FE of serologically positive or negative heifers for BLV and of cows that were serologically positive but clinically negative, did not endanger the heifers. Cross reaction was not observed between serum containing antibodies for BLV and serum containing antibodies for bovine diarrhea virus. (5 Refs) (In POR)

CYTOGENETIC AND MORPHOLOGIC STUDIES

13. DIAGNOSTIC AND PROGNOSTIC SIGNIFICANCE OF CHROMOSOME ABNORMALITIES IN MARROW AND MITOGEN RESPONSE OF LYMPHOCYTES OF ACUTE NONLYMPHOCYTIC LEUKEMIA.

Shiraishi Y, Taguchi H, Niiya K, Shiomi F, Kikukawa K, Kubonishi S, Ohmura T, Hamawaki M, Ueda N
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Cancer Genet Cytogenet; 5(1):1-24 1982

Chromsomes of bone marrow from 28 patients with acute nonlymphocytic leukemia (ANLL) (26 with AML, 2 with AMMoL), 19 of whom had chromosome abnormalities, were studied; 11 cases exhibited previously unreported karyotypic abnormalities. The marrows of two cases had 8-21 translocations associated with an iso-X chromosome in the female patient and with 9q13-and a missing Y in the male patient. Usually, AML patients with an 8-21 translocation have been considered to have a good prognosis; however, our cases had rather short survival times. Therefore, the prognosis of AML with an 8-21 translocation but associated with other abnormalities is still not clear. Centromere spreading (CS), which was originally reported in marrow cells of megaloblastic anemia (B12 and folic acid deficiency), was detected in leukemic cells, disappeared during remission, and reappeared on relapse. These findings suggest that CS may be a new type of abnormality in AML. In two patients with atypical hypoplastic anemia and hemolytic anemia, chromosome abnormalities were detected at the anemic stage. One case with CS was associated with atypical hypoplastic anemia and developed AML after 1 yr; the other with 48,XY,+i(1q),+3,+12 and-14 had hemolytic anemia and develop ed AMMoL 3 wk later. Interestingly, identical clones were detected both before and after the clinical diagnosis of leukemia. These cases strongly support the concept that some chromosome abnormalities precede the clinical manifestations of leukemia. The present study also revealed that lymphocytes in ANLL respond poorly to PHA in the presence of high numbers of blasts but do respond well to mitogens during remission. Therefore, the response of lymphocytes to PHA may serve as one criterion for determining remission. (Author abstract) (15 Refs)

14. CYTOGENETIC STUDIES IN 56 CASES WITH PH(1)-POSITIVE HEMATOLOGIC DISORDERS.

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Cancer Genet Cytogenet; 5(1):37-49 1982

Karyotypes were examined in 56 cases of Ph(1)-positive hematologic disorders based on direct examination of bone marrow material and culture of blood for 24 hr without phytohemagglutinin (PHA). Various banding techniques (Q, followed by R or C, where necessary) were used. The series of patients consisted of 21 females and 35 males with the ages ranging from 3 to 72 yr. In three cases, the clinical and hematologic picture at the time of diagnosis and karyotyping was not compatible with chronic myeloid leukemia (CML): one case had acute myeloblastic leukemia (AML), another acute lymphoblastic leukemia (ALL) and the third subacute myeloid leukosis. The results are as follows: In three cases (2 females, 1 male), no Ph1 translocation could be demonstrated in any of the metaphases either with Q- or R-banding. In 50 cases (19

female, 31 male), a standard Ph1 translocation, t(9;22)(q34;q11), was observed. In two of these cases, ages 45 and 47, the Ph1 translocation was accompanied by loss of the Y chromosome in all the metaphases examined. Finally, in three cases (all male), variant Ph(1)-translocations were found: t(7;9)(9;22)(q35?;q31?;q11), t(3;9;22)(p21;q34;q11), and t(1;9)(9;22)(q21;q34;q11). (Author abstract) (21 Refs)

15. THE 5Q-MINUS SYNDROME - A CHROMOSOMAL ABERRATION WITH CHARACTERISTIC HEMATOLOGICAL PICTURES: PRELEUKEMIA?.

Mueller RA, Auf der Maur P, Beck EA, Deubelbeiss K, Bucher U
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Schweiz Med Wochenschr; 112(7):242-252 1982

The case of a 74-yr-old woman with macrocytic, refractory anemia, typical changes in the bone marrow and a 5q-chromosome in bone marrow cells is presented and the literature of this newly described hematological disorder is reviewed. The syndrome is characterized by partial deletion of the long arms of a chromosome No 5 in bone marrow cells. The chromosomal anomaly is acquired and originates most probably from a pluripotent hematologic stem cell. Hematologic changes are (1) macrocytic, refractory anemia , (2) low to normal leukocyte counts, (3) normal to increased platelet number with marked anisocytosis and a high proportion of megathrombocytes, (4) normal to hypoplastic erythropoiesis and generally small megakaryocytes with nonlobulated nuclei in the bone marrow. In most of the reported cases (16 out of 19) with isolated 5q-anomaly, the clinical picture and laboratory findings remained stationary during a follow-up period of up to 6 yr. In only 2 out of 19 cases did acute leukemia develop. In the presence of additional chromosomal abnormalities, all the cases developed acute leukemia and especially acute myelogenous leukemia. The diagnosis of 5q-syndrome in patients with refractory anemia is of prognostic significance, since it renders possible early recognition of a potentially malignant disorder and early detection of leukemic transformation. (Author abstract) (53 Refs) (In GER)

16. HIGH-RESOLUTION ANALYSIS OF CHROMOSOME MARKERS IN BURKITT LYMPHOMA CELL LINES.

Zhang S, Zech L, Klein G
Dept. Medical Cell Genetics, Medical Nobel Inst. Karolinska Institutet, S-104 01 Stockholm, Sweden
Int J Cancer; 29(2):153-157 1982

Using a high-resolution chromosome banding technique, which provided more elongated and distinctly banded chromosomes, some new evidence was obtained for localization of break points in Burkitt lymphoma marker chromsomes. As a result, the characteristic translocation between chromosomes 8 and 14 was designated as t(8;14) (q24.1;q32.5) and the deletion of chromosome 15 was designated as del(15) (q13q15). (Author abstract) (19 Refs)

17. CHROMOSOME ANALYSES IN MULTIPLE MYELOMA.

Balogh E, Kaszas I, Krizsa F, Fleischmann T
II. Belgyogyaszati Osztaly, Szegedi Orvostudomanyi Egyetem, Szeged, Hungary
Orv Hetil; 123(1):35-37 1982

Chromosome analyses were performed in bone marrow cells from 10 patients (4 men and 6 women, 35-75 yr old) with multiple myeloma (MM). Four of the 10 patients had been pre-treated; their treatment had consisted of chemotherapy. The type of the serum paraprotein was IgG-kappa in six patients, IgG-lambda in three and IgA-lambda in one. Bence-Jones proteinuria was seen in 4/10 patients. The skeletal system was affected with certainty in five patients, probably in one. The bone marrow was involved in all 10 patients. The chromosome count of the main cell line was 46 in nine patients, 47 in one. Clonal aberrations (+17,-18; 14 micron+, M,-19, +20, and 17p+) were found in five patients. Random anomalies were seen in six patients. The random anomalies were mostly numerical changes in the karyotypes. (15 Refs) (In HUN)

18. KLINEFELTER'S SYNDROME AND ACUTE NON-LYMPHOCYTIC LEUKEMIA.

Muts-Homsma SJ, Muller HP, Geraedst JP
Dept. Medicine, Div. Haematology, Univ. Hosp., NL-2333 AA Leiden, The Netherlands
Blut; 44(1):15-20 1982

Case reports are presented of five patients (30-64 yr old) with Klinefelter's syndrome (KS) among 51 male adult patients with acute non-lymphocytic leukemia (ANLL). Peripheral blood was cultured for 24 hr without stimulation and for 72 hr in the presence of phytohemagglutinin (PHA). All chromosome analyses were performed after G-banding. All of the patients had a 47,XXY karyotype; one patient showed the same karyotype when bone marrow cells were cultivated with or without PHA stimulation. Cultures of one patient showed three different cell lines, two of which contained acquired chromosome anomalies, +8 and 20 q-,+21. The incidence of KS in this series (1:10) was much higher than that in the combined data of six newborn studies with 35 cases of the KS chromosome abnormality among 37,779 males (about 1:1,000). It is concluded the Klinefelter's syndrome probably predisposes to the development of ANLL, although the causative factor(s) are unknown. (23 Refs)

19. CHROMOSOMES IN LEUKEMIA AND LYMPHOMA WITH SPECIAL EMPHASIS ON METHODOLOGY.

Testa JR, Rowley JD
Cytogenetics Lab., Section Hematology and Oncology, Dept. Medicine, Univ. Chicago, Chicago, IL
Methods Hematol; 2:184-202 1981

Methodology of chromosome analysis in diagnosis of leukemia is presented. Cells for study may be cultured from cells from bone marrow aspirate, bone core biopsy, peripheral blood, lymph nodes, spleen, or effusions. Specimens may be stained by conventional, quinacrine-banding, Giemsa-banding, reverse-banding, or C-banding techniques. Chromosome abnormalities of chronic myeloid leukemia, acute leukemia, malignant lymphoma, and multiple myeloma are summarized. (48 Refs)

20. MEGAKARYOBLASTIC TRANSFORMATION OF CHRONIC MYELOGENOUS LEUKEMIA.

Williams WC, Weiss GB
Div. Hematology-Oncology, Univ. Texas Medical Branch, Galveston, TX, 77550
Cancer; 49(5):921-926 1982

A 52-yr-old man with Ph1-positive chronic myelogenous leukemia (CML) developed a blastic transformation in which the predominant cell type was micromegakaryocytes. He did not respond to treatment. A review of the 15 previously reported cases of patients with circulating megakaryocyte abnor-

malities in association with either CML or a Ph1 chromosome positive myeloproliferative disorder suggests a female predominance rather than the usual male predominance of CML. Survival of the six patients reported as megakaryoblastic transformation of CML as well as this patient was poor. (Author abstract) (38 Refs)

21. QUANTITATIVE EVALUATION OF ERYTHROPOIETIC ACTIVITY IN DYSMYELOPOIETIC SYNDROMES.

Cazzola M, Barosi G, Berzuini C, Dacco' M, Orlandi E, Stefanelli M, Ascari E
Patologia Medica 1, Policlinico S. Matteo, 27100 Pavia, Italy
Br J Haematol; 50(1):55-62 1982

Based on the morphological appearances of the bone marrow and peripheral blood, 43 patients with dysmyelopoietic syndromes were categorized into four types: refractory anemia with excess of blasts, chronic myelomonocytic leukemia, primary acquired sideroblastic anemia and refractory anemia with cellular marrow, with excess of blasts and/or ring sideroblasts. Ferrokinetics allowed three distinct groups of patients to be defined. All cases of refractory anemia with excess of blasts and chronic myelomonocytic leukemia were classified in the same group. They were characterized by relative marrow failure and had a high likelihood of developing acute leukemia. At the other end of the spectrum, individuals with primary acquired sideroblastic anemia had high erythropoietic activity which was largely ineffective. They had a benign clinical course without evidence of leukemic transformation. In the middle group, in terms of erythropoietic activity, lay patients with refractory anemia with cellular marrow and a few individuals with primary acquired sideroblastic anemia. Their clinical course and risk of developing acute leukemia were intermediate between the other two groups. These findings indicate that separate entities may exist within the spectrum of dysmyelopoietic syndromes. In clinical practice, they may be recognized by morphological studies and other simple laboratory means. (Author abstract) (22 Refs)

22. REGRESSING ATYPICAL HISTIOCYTOSIS: A CUTANEOUS PROLIFERATION OF ATYPICAL NEOPLASTIC HISTIOCYTES WITH UNEXPECTEDLY INDOLENT BIOLOGIC BEHAVIOR.

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Dept. Dermatology, Univ. Hosp., Box 98, 420 Delaware St., SE, Minneapolis, MN, 55455
Cancer; 49(5):959-970 1982

Regressing atypical histiocytosis (RAH) of skin is a cutaneous noduloulcerative proliferation of atypical neoplastic histiocytes with concomitant polymorphous inflammation, frequently pronounced epidermal hyperplasia, and an unexpectedly indolent biologic course. Spontaneous regression and recurrence without systemic spread were the course in follow-up periods of over 6 yr. Histopathologically, characteristic-appearing atypical mononuclear and multinucleated 'RAH' cells showed erythrophagocytosis as well as ultrastructural, surface marker, and enzyme cytochemical features indicating histiocytic differentiation. Cytogenetic analysis showed aneuploidy and several marker chromosomes including 14q+. Its benign biologic course clearly distinguished this entity from malignant histiocytosis, large cell lymphoma, and Hodgkin's disease. The histiocytic atypical cells further distinguished it from the T-cell lesions of the skin, such as mycosis fungoides and lymphomatoid papulosis. This entity is readily confused with malignant lymphoreticular disease, melanoma, or squamous carcinoma. (Author abstract) (68 Refs)

23. CEREBROSPINAL FLUID CYTOLOGY IN HISTIOCYTIC PROLIFERATIVE DISORDERS.

Hamilton SR, Gupta PK, Marshall ME, Donovan PA, Wingard JR, Zaatari GS
Dept. Pathology, Johns Hopkins Hosp., 600 North Wolfe St., Baltimore, MD, 21205
Acta Cytol (Baltimore); 26(1):22-28 1982

Morphologically atypical histiocytes were observed in the cerebrospinal fluid (CSF) of five patients with histiocytic proliferative disorders, including one each classified as Letterer-Siwe disease and Hand-Shuller-Christian disease and three as malignant histocytosis. In all of these patients except the one with Letterer-Siwe disease, neurologic examination, CSF leukocyte count and protein and glucose concentrations were normal. Necropsy studies in three fatal cases (1 patient with Letterer-Siwe disease and 2 with malignant histiocytosis) demonstrated leptomeningeal involvement by atypical histiocytes in all three and brain involvement in the patient with Letterer-Siwe disease. These observations suggest that cytologic examination of CSF is warranted in patients with histiocytic proliferative disorders and may be reliable in documenting central nervous system, particularly leptomeningeal, involvement. The atypicality of the histiocytes in the CSF, however, was not indicative of the classification of the histiocytic proliferative disorder. Because the patient with Hand-Schuller-Christian disease continues to have a normal neurologic examination 7 yr after abnormal histiocytes were initially detected in his CSF, we believe that the clinical condition of the patient and classification of the histiocytic proliferative disorder are of primary importance for initiating aggressive therapy directed at the central nervous system. (Author abstract) (13 Refs)

BIOCHEMICAL, IMMUNOLOGICAL AND OTHER CELL BIOLOGY STUDIES

24. CELL-MEDIATED AND HUMORAL IMMUNITY IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA.

Jagielski P, Litwin J, Rokicka-Milewska R, Derulska D, Madalinski K
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Pediatr Pol; 56(9):993-1001 1981

The cell-mediated and humoral immunity was studied in 50 children (2-14 yr old) with acute lymphoblastic leukemia (ALL) during exacerbations and remissions under treatment and in 9 subjects (12-25 yr old) during long-term remission from ALL without treatment. The tests performed included the E rosette test, the spontaneous and phytohemagglutinin (PHA)-, concanavalin A (Con A)- and pokeweed mitogen (PWM)-stimulated blast transformation tests, and the determination of the serum immunoglobulin levels. The E rosette formation was reduced in most patients regardless of the phase of the disease and of the length of treatment. The blast transformation tests were more differentiated: the spontaneous blast transformation of the lymphocytes was increased during the acute phase of the disease, and the PHA-induced blast trans formation was decreased during remission. Significant reduction of the blast transformation after stimulation with all three

mitogens, and reduced IgA and IgM levels were observed during the second yr of treatment. The only immune deficiency found in the nine patients in long-term remission after withdrawal of the treatment was reduced E rosette formation. (25 Refs) (In POL)

25. CORRELATION BETWEEN MIXED LYMPHOCYTE CULTURES AND ANTI-EPSTEIN BARR VIRUS (EBV) ANTIBODIES IN HODGKIN'S DISEASE AND NON HODGKIN LYMPHOMA PATIENTS.

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Instituto de Investigaciones Hematologicas, Academia Nacional de Medicina, Pacheco de Melo 3081, 1425 Buenos Aires, Argentina
Biomedicine [Express]; 35(5):153-156 1981

Cellular and humoral immunity was examined in Hodgkin's disease and non Hodgkin lymphoma (33) patients and compared with a normal group. Mixed lymphocyte cultures (MLC) were used as a parameter for cell mediated immunity and anti-Epstein Barr virus (EBV) antibodies for specific humoral immunity. High stimulation indices coincided with low anti-VCA and anti-EBNA titers in the control group ($r = -0.343$). This negative correlation was not found in non Hodgkin lymphomas and was substantially lower ($r = -0.142$) in Hodgkin's disease. The alterations in immunoregulatory mechanisms in these patients are discussed. (Author abstract) (29 Refs)

26. DETERMINATION OF ULTRASTRUCTURAL PEROXIDASES AND IMMUNOLOGIC MEMBRANE MARKERS IN THE DIAGNOSIS OF ACUTE LEUKEMIAS.

Marie JP, Perrot JY, Boucheix C, Zittoun J, Matyre MC, Kayibanda M, Rosenfeld C, Mishal Z, Zittoun R
Service d'Hematologie, Hotel Dieu, 1 place du Parvis Notre Dame, 75181 Paris Cedex 04, France
Blood; 59(2):270-276 1982

Detection of membrane markers and ultrastructural peroxidase activity was carried out on the blasts of 16 apparently nonmyeloid adult acute leukemias. These patients were selected from 73 adult leukemic patients by the negativity of their routine cytochemical myeloid markers: ie, myeloperoxidase, cholesterase activity, and Sudan Black B staining. B and T acute lymphoid leukemias (ALL) were excluded from the study. After concurrent testing from human T lymphocyte antigen (HuTLA), common ALL antigen (cALL), Ia-like antigens, and peroxidase activity at the electron microscopic level (POEM), only two patients remained undifferentiated (cALL-, POEM-). Two other cases were classified as following: six common ALL (cALL+, POEM-), one pre-T-ALL (cALL+, HuTLA+, POEM-), five very poorly differentiated acute myelogenous leukemia (AML) (cALL-, POEM+), and two mixed leukemias (cALL+, POEM+). Terminal deoxynucleotidyl transferase activity (TdT) was measured in seven cases and was found to be present at high levels in four cases of cALL and in the two cases of acute undifferentiated leukemias (AUL); it was absent in two cases of AML. Cytogenetic analysis had showed that 2 of the cALLs, three of the AMLs, and the two mixed leukemias were Ph1+. We conclude that POEM detection is useful in apparently nonmyeloid leukemias with negative immunologic lymphoid markers, and that the existence of a Ph+ chromosome should be investigated, particularly in the unusual case of mixed (lymphoid-myeloid) acute leukemia. (Author abstract) (24 Refs)

27. CHARACTERIZATION OF NORMAL AND MALIGNANT HUMAN LYMPHOID CELL POPULATIONS.

Ford RJ
Dept. Pathology, Univ. Texas M.D. Anderson Hosp. and Tumor Inst., Houston, TX
Cancer Bull; 33(6):255-260 1981

Characterization of human lymphoid cell populations with both conventional cell membrane markers and monoclonal antibodies is reviewed. The most reliable human T-cell marker is the sheep red blood cell rosette assay, usually performed with neuraminidase-treated sheep RBC. The cell-surface immunoglobulin receptor is the most reliable human B-cell marker; others include the membrane receptor for Epstein-Barr virus and the mouse RBC membrane receptor. Monocytes and macrophages may be identified and separated by means of the phagocytosis of latex particles; in addition, enzymes such as alpha-naphthylacetate esterase are relatively specific for the monocyte/macrophage system when present in a diffuse cytoplasmic staining pattern. Hybridoma technology has given rise to the use of mouse monoclonal antibodies for identifying various types of human lymphocytes. Panels of monoclonal antibodies with defined specificities will probably make conventional cell markers obsolete in the near future. Conventional immunologic markers for a number of neoplastic lymphoid cells, including T- and B-cell lymphomas and leukemias and histiocytic lymphomas, are discussed. Recent studies concerning the use of monoclonal antibodies for differentiation of lymphoma and lymphocytic leukemia subtypes are described. (38 Refs)

28. PRODUCTION OF IMMUNOREACTIVE CALCITONIN BY MYELOID LEUKAEMIA CELLS.

Fox R, Oscier DG, Hillyard CJ, Incarbone E, McIntyre I, Goldman JM
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Br J Haematol; 50(2):215-223 1982

Raised plasma levels of immunoreactive human calcitonin (i-HCT) have been found in patients with chronic granulocytic leukemia (CGL) in chronic phase and myeloblastic transformation and in patients with acute myeloid leukemia at presentation and in relapse. In CGL levels were significantly higher in myeloblastic transformation than in the chronic phase. Leukemia cells were cultured in a short-term liquid culture system in which little cell proliferation occurs and in a two layer blast-cell colony system which permits blast-cell proliferation. i-HCT was identified in supernatant media from cells cultured in both systems but levels were substantially higher in media collected from cells cultured in the latter system. These results suggest that i-HCT is synthesized by proliferating blast cells. (Author abstract) (7 Refs)

29. EFFECT OF LEUKAEMIA ON THE CONCENTRATION OF SOME TRACE ELEMENTS IN HUMAN WHOLE BLOOD.

Mangal PC, Sharma P
Dept. Biophysics, Panjab Univ., Chandigarh 160014, India
Indian J Med Res; 74:559-564 1981

Concentrations of eight trace elements viz Fe, Zn, Co, Cr, Se, Rb, Sc and Hg were determined in the normal and leukemic human whole blood. Neutron activation technique incorporating a Ge (Li) detector having 60 cm3 active volume and a 4,096 channel pulse height analyzer was used for this pur-

pose. There was a significant decrease in the concentrations of Co, Cr, Rb and Fe in leukemic blood. The concentrations of Zn and Sc were decreased by small amounts which were not statistically significant. The concentrations of Se and Hg were increased in leukemia. When concentrations of these trace elements in leukemic blood were compared with the leukocyte cell counts in each subject, it was found that the concentrations of Fe, Zn, Co, Cr and Sc decreased and those of Se and Rb increased monotonically with increase in the leukocyte cell counts. The increase in the level of Rb and the decrease in the level of Hg as a function of leukocyte cell counts was in contradiction to the changes in the concentrations of these elements in leukemia, as compared to those in the normal blood samples. The study thus suggests some special role of Rb and Hg - both non-essential elements, in the initiation and progress of leukemia. (Author abstract) (9 Refs)

30. MOUSE BRAIN: AN IMMUNOLOGICALLY PRIVILEGED SITE FOR NATURAL RESISTANCE AGAINST LYMPHOMA CELLS.

Circolo A, Bianhci R, Nardelli B, Rivosecchi-Merletti P, Bonmassar E
(c/o Bonmassar) Inst. Pharmacology, Univ. Perugia, Via del Giochetto, Perugia 06100, Italy
J Immunol; 128(2):556-562 1982

Localized (ie, organ-restricted) resistance against murine lymphoma cells has been described in spleen, liver, and lung of irradiated mice. This natural resistance (NR) is distinguishable from the T-dependent classical graft response (CGR) because it does not require a sensitization period and is detectable in lethally irradiated hosts and in intact or lethally ir adiated 'nude' mice. The present study deals with classical graft response and natural resistance against lymphoma cells in mouse brain, evaluated in terms of either survival times or extent of lymphoma cell proliferation measured by the percentage of 125IUdR uptake. The results show the following: (a) CGR was easily detected in the brain of allogeneic nonirradiated recipients by using either parameter. CGR was easily abrogated by total-body irradiation and was absent in 'nude' recipients when tested by the 125IUdR uptake technique. (b) No difference in the growth patterns of H-2b lymphoma cells was detected in the brain of irradiated histocompatible or Hh-incompatible hybrid (H-2b/H-2d) or allogeneic (H-2b, H-215) mice or Hh-compatible H-2h2 hosts inoculated intracerebrally (ic) with the tumor. On the contrary, strong resistance to lymphoma graft was confirmed in the spleen of irradiated Hh-incompatible recipients inoculated iv with the tumor. (c) No impairment of splenic resistance against lymphoma cells was afforded by the simultaneous administration of the same tumor into the brain, thus ruling out the possibility that the ic challenge with lymphoma cells abrogated NR of the host. (d) Mortality studies in nonirradiated Hh-incompatible hybrid or nude mice suggested that only marginal NR could be detected in mouse brain. These data suggest that mouse brain can be considered an 'immunologically privileged' site for NR more than for CGR, and provide the immunologic bases for explaining the successful take of xenogeneic lymphoid tumors in the brain of nude mice. In addition, they do not support the hypothesis that NR could play a major role in the immunosurveillance mechanisms against tumors at brain level in the mouse. (Author abstract) (59 Refs)

EXPERIMENTAL STUDIES INVOLVING CHEMICAL AGENTS AND IRRADIATION

31. ATTEMPTED TUMOR INDUCTION WITH AGARITINE IN MICE.

Toth B, Raha CR, Wallcave L, Nagel D
Eppley Inst. for Res. in Cancer, Univ. Nebraska Medical Center, Omaha, NE, 68105
Anticancer Res; 1(5):255-258 1981

The effect of chronic administration of agaritine (AG), cultivated from Agaricus bisporus, to Swiss albino mice was investigated. Animals received a 0.0625% soln in drinking water for life beginning at 48 days of age (Group 1: 50 females, 50 males; av daily intake of AG of 3.15 mg/female mouse and 3.94 mg/male mouse); or a 0.03125% soln beginning at 44 days of age (Group 2: 50 males, av daily intake 2.68 mg/mouse). Group 3 contained 100 female and 100 male untreated control mice. Males treated with the 0.0625% soln had significantly shorter survival times than controls. Lung tumors developed in 26% of females and 12% of males in Group 1, in 16% of males in Group 2, and in 29% of females and 19% of males in Group 3. Malignant lymphomas developed in 12% of females and 2% of males in Group 1, in 2% of males in Group 2, and in 15% of females and 10% of males in Group 3. Blood vessel tumors developed in 4% of females and 4% of males in Group 1, in 10% of males in Group 2, and in 7% of females and 5% of males in Group 3. Thus, under these conditions, AG had no apparent carcinogenic effect. A substantial number of mice developed convulsions and died of seizures in this study. (30 Refs)

EXPERIMENTAL STUDIES: DNA TUMOR VIRUSES

32. CELL SURFACE PROPERTIES OF HLA ANTIGENS ON EPSTEIN-BARR VIRUS-TRANSFORMED CELL L INES.

Smith LM, Petty HR, Parham P, McConnell HM
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Proc Natl Acad Sci USA; 79(2):608-612 1982

A number of monoclonal antibodies have been used to investigate the distributions and rates of lateral motion of the HLA-A,B, and -DR antigens on several Epstein-Barr virus-transformed B-cell lines. The lateral diffusion coefficients (D) of fluorescein conjugates of the monoclonal antibodies bound to the cell surface were determined by fluorescence recovery after pattern photobleaching. Ds of HLA-A and -B were found to be comparable and of the order of 10(-9) to 10(-10) cm2/sec for each of the seven monoclonal antibodies and four cell lines examined. The HLA antigens appear to be monomeric on the cell surface based on experiments using mixtures of arsanilic acid-conjugated and fluorescein-conjugated antibodies. Four monoclonal antibodies against DR antigens were examined. Two of these, Genox 3.53 and L243, labeled the cell surface uniformly and gave Ds comparable to those obtained for the HLA-A and -B antigens. The other two, DA2 and 2.06, rapidly patched on the cell surface and were immobile. The DA2, L243, and Genox 3.53 antibodies bound outside of the caps formed with the arsanilic acid-conjugated 2.06 antibody and a second-step rhodamine-conjugated rabbit anti-arsanilate antibody. This is consistent with recent biochemical evidence that

there are multiple distinct antigens coded for by the HLA-DR region. (Author abstract) (63 Refs)

33. INSULIN RECEPTORS ON HUMAN LYMPHOID LINES OF B-CELL ORIGIN.

Aman P, Lundin G, Hall K, Klein G
Dept. Tumor Biology, Karolinska Institut, S-104 01 Stockholm, Sweden
Cell Immunol; 65(2):307-316 1981

Human lymphoid lines derived from normal or neoplastic B cells were assayed for insulin binding. 125I-Labeled insulin was allowed to bind to cells. Bound radioactivity which was inhibited with unlabeled insulin was regarded as specific binding. Among 46 lines tested, 43 bound more insulin than normal peripheral B lymphocytes. The majority of the lines resembled activated lymphocytes, with regard to their insulin binding. More mature cells represented by EBV-transformed lines of normal origin, bound more insulin than the less differentiated Burkitt lymphoma lines. However, even the latter bound significantly more insulin than peripheral blood lymphocytes. (Author abstract) (35 Refs)

34. B LYMPHOBLAST ANTIGEN (BB-1) EXPRESSED ON EPSTEIN-BARR VIRUS-ACTIVATED B CELL BLASTS, B LYMPHOBLASTOID CELL LINES, AND BURKITT'S LYMPHOMAS.

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J Immunol; 128(2):823-827 1982

Two new cell surface antigens expressed on B lymphoblastoid cell lines (B-LCL) w ere defined with cytotoxic mouse monoclonal antibodies. One marker, BB-1 (for B lymphoblast antigen-1), was detected on human and nonhuman primate B-LCL, Epstein-Barr virus (EBV)-activated B cell blasts, most Burkitt's lymphomas, and Ia+ B lymphoblast-like myelomas. Polyclonal B cell activators such as pokeweed mitogen (PWM) and lipopolysaccharide (LPS) also induced the expression of BB-1 on immunoglobulin (Ig)-positive cells.In contrast, BB-1 could not be detected on normal lymphoid tissues by complement-dependent cytotoxicity and immunofluorescence (IF) assays or by analysis with a fluorescence-activated cell sorter (FACS). T cell blasts, T cell leukemias, and pre-B cell or erythroblastic leukemia cell lines were also BB-1 negative. Of particular interest was the finding that BB-1 was expressed on the Jijoye lymphoma but only marginally on a subline of Jijoye, P3HR-1, that lacks receptors for EBV and produces a defective virus incapable of transforming lymphocytes. A second lymphoblast antigen (LB-1) unlike BB-1, was present on both T and B cell blasts and virus-transformed T- and B-LCL but not on normal lymphoid tissues. (Author abstract) (50 Refs)

35. CORRELATION BETWEEN VARIANT TRANSLOCATION AND EXPRESSION OF IMMUNOGLOBULIN LIGHT CHAINS IN BURKITT'S LYMPHOMAS AND LEUKEMIAS.

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C R Acad Sci [III] (Paris); 293(8):427-429 1981

Expression of immunoglobulins (IG) in Burkitt's lymphomas (19 lines) and leukemias (1 line) are discussed in relation to observed chromosome abnormalities. Of the 19 lymphoma lines, 12 were non-endemic and 7 did not contain the Epstein Barr virus. IG light chains produced varied according to the type of translocation. In 17/18 cases with translocation t(8;14), the light chains of surface and cytoplasmic IG were type kappa (9 cases) or type gamma (8 cases). The cells of patient 18 did not express any detectable light chains. In 3/5 cases of translocation t(2;8), the light chains were type kappa with light chain expression in 1/3; the two other cell lines exhibited a pre-B phenotype. Of six cases with translocation t(8;22), IG with gamma chains were found in 5 and a pre-B phenotype in the sixth. IgM, sometimes associated with IgD, was found in 17/19 cell lines; two cell lines were characterized by monoclonal gamma IgG (translocation t(8;14) in one case and t(8;22) in the other). The results indicated the existence of a relationship between translocations t(2;8) and t(8;22) and light chain expression: kappa in the case of t(2;8) and gamma in the case of t(8;22). (12 Refs) (In FRE)

36. IDENTIFICATION OF EPSTEIN-BARR VIRUS STRAIN DIFFERENCES WITH MONOCLONAL ANTIBODY TO A MEMBRANE GLYCOPROTEIN.

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Proc Natl Acad Sci USA; 79(2):616-620 1982

Two monoclonal antibodies directed against Epstein-Barr virus (EBV)-induced membrane antigens (MA) were isolated in this study. One of the monoclonal antibodies, designated 2F5.6, was an IgG2 which, as detected by membrane and fixed cell immunofluorescence, reacted with MA-positive lymphoblastoid cell lines that produced transforming EBV but not with the MA-positive P3HR-1 cell line that produced the lytic, nontransforming strain of this virus. This antibody precipitated the Mr 320,000/350,000 glycoprotein from B-95 virus infected cultures and the Mr 300,000 and 220,000/250,000 glycoproteins from Raji cells superinfected with P3HR-1 virus but did not precipitate any of these EBV-specific glycoproteins from the P3HR-1 cell line. In contrast, the second monoclonal antibody, IgM designated B10.3, reacted with all virus-producing cell lines including the P3HR-1 cell line. The identity of the glycoprotein that serves as the target for this antibody is still unknown. Neither antibody had neutralizing activity against the B-95 or P3HR-1 strain of EBV. These results indicated that the 2F5.6 monoclonal antibody was directed against an antigenic determinant on the major membrane glycoprotein which is common to transforming strains of EBV but absent from the lytic P3HR-1 strain whereas the B10.3 monoclonal antibody was directed against a group-specific EBV-induced membrane determinant. (Author abstract) (25 Refs)

37. CELL SURFACE GLYCOPROTEIN PATTERNS OF TWO EBV-NEGATIVE LINES AND THEIR EBV CONVERTED SUBLINES.

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Dept. Tumor Biology, Karolinska Institutet, S-104 01 Stockholm, Sweden
Intervirology; 16(3):142-148 1981

Cell surface galactosyl-glycoprotein patterns were compared between Ramos and BJAB, two Epstein-Barr virus (EBV)-negative Burkitt lymphoma lines, and their acutely EBV-superinfected and stably EBV-converted derivatives. A major difference between Ramos and its EBV-infected variants was the appearance of a 69,000 mol wt galactosyl-glycoprotein (GP 69)

in the latter. The same phenomenon was found in BJAB along with the additional appearance of a 71,000 mol wt galactosyl-glycoprotein (GP71) in the EBV-infected cells. GP71 was present in Ramos and in its EBV-converted derivatives. (Author abstract) (23 Refs)

38. CHARACTERIZATION OF THE MAJOR EPSTEIN-BARR VIRUS-SPECIFIC RNA IN BURKITT LYMPHOMA-DERIVED CELLS.

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Imperial Cancer Res. Fund Lab., London WC2A 3PX, England
J Virol; 41(2):376-389 1982

Cytoplasmic RNA prepared from five lymphoid cell lines and a Burkitt lymphoma biopsy was radioactively labeled in vitro and hybridized to cloned EcoRI restriction endonuclease fragmen ts of B95-8 Epstein-Barr virus DNA. The results confirmed that the most abundant cytoplasmic RNA species in such cells is specified by a small region of the genome defined by the EcoRI J fragment. Detailed mapping experiments precisely localized these transcripts within the sequence of the rightmost one-third of the EcoRI J fragment. DNA sequencing suggested that this region of the Epstein-Barr virus genome is unable to code for protein. The major early transcripts consisted of two non-polyadenylated RNA species, each about 170 nucleotides in length. They were both transcribed off the same strand of the DNA and showed significant sequence homology with each other. The coding sequences of the two small RNAs contained potential intragenic control regions for RNA polymerase III. (Author abstract) (53 Refs)

39. EPSTEIN-BARR VIRUS SUSCEPTIBILITY OF B CELLS CORRELATES TO THE PRESENCE OF COMPLEMENT RECEPTORS BUT NOT SURFACE IMMUNOGLOBULINS.

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Intervirology; 16(2):118-122 1981

Nuclear antigen (EBNA) inducibility by Epstein-Barr virus (EBV) was assessed in relation to the presence of complement (C3) receptors and surface immunoglobulins (SIg) on leukemic lymphocytes. When erythrocyte-antibody-complement complex (EAC)-positive, SIg-negative B cells were exposed to EBV, EBNA synthesis occurred with a high frequency. In contrast, no significant EBNA induction was evident in SIg-positive, EAC-negative B cells. Cells possessing both markers were EBV-infectable, in proportion to the frequency of EAC-rosette formation. These data seem to indicate that EBV susceptibility of human B cells is closely related to the presence of C3 receptors but not SIg. Leukemic T cells and myelogenous leukemia cells were not EBV-susceptible, although some cells were significantly positive for C3 receptors. (Author abstract) (15 Refs)

40. EFFECTS OF N-BUTYRATE ON EPSTEIN-BARR VIRUS-CARRYING LYMPHOMA LINES.

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J Gen Virol; 58(part1):163-171 1982

The compound n-butyrate has been shown to induce Epstein-Barr virus (EBV) antigen synthesis in certain EBV-carrying lymphoma lines. We have studied the effect of n-butyrate on two EBV-positive Burkitt lymphoma lines by immunofluorescence and electron microscopy. In the producer line P3HR-1, the drug induced not only early antigen (EA) and virus capsid antigen (VCA) synthesis, as shown before, but also increased the number of cells containing virus particles. The transition from VCA expression to the formation of virus particles was much more effective in treated cells than in EBV antigen-producing cells of the same line. The productive cycle was associated with the development of characteristic morphological changes. In the non-producer Raji cells, n-butyrate induced EA in only a minor fraction of the cells. There were, however, clear signs of differentiation in the direction of plasma cells. Two days after the addition of n-butyrate 80% of the Raji cells could be classified as plasmablasts. After 72 hr, 20% of the cells appeared as typical plasma cells. (Author abstract) (33 Refs)

41. DNA-POLYMERASE INDUCED BY HERPESVIRUS PAPIO (HVP) IN CELLS OF LYMPHOBLASTOID CULTURES DERIVED FROM LYMPHOMATOUS BABOONS. - REPORT V.

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Exp Pathol; 20(1):51-57 1981

A new DNA-polymerase was found in the cells of suspension lymphoblastoid cultures which produce lymphotropic baboon herpesvirus (HVP). This enzyme was isolated in a partially purified form. Some of its properties vary from those of other cellular DNA-polymerases. HVP-induced DNA-polymerase has a molecular weight of 160,000 and sedimentation coefficent of about 8 S. The enzyme is resistant to high salt concentration and N-ethylmaleimide, but it is very sensitive to phosphonoacetate. It effectively copies 'activated' DNA and synthetic deoxyribohomopolymers. Attempts to reveal the DNA-polymerase activity in HVP virions were unsuccessful. (Author abstract) (15 Refs)

42. THE MECHANISM OF GENETIC RESISTANCE TO MAREK'S DISEASE IN CHICKENS.

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Int J Cancer; 29(2):169-174 1982

Genetic resistance to Marek's disease in RPL line-6 chickens is expressed not only at the level of host immunological responses against virus and tumor antigens, but also at the level of target lymphoid cells for virus infection and transformation. The nature of the target cell involved was investigated. Spleen cells from susceptible line-7 chickens adsorbed more Marek's disease virus and turkey herpesvirus in vitro than line-6 spleen cells. In the case of Marek's disease virus this was reflected in the replicative ability of the virus in vivo. Transplantation of thymus fragments from 1-day-old line-7 chickens into thymectomized line-6 chickens conferred a high degree of susceptibility on the latter, but the transplantation of spleen or bursa fragments had no significant effect. The reverse procedure, ie grafting of line-6 thymi into line-7 chickens, did not diminish the susceptibility of the recipients. In each treatment group the observed titers of leukocyte-associated viremia correlated with the susceptibility of the group to Marek's disease. Histologically the grafted thymus fragments became depleted of lymphocytes immed iately after transplantation. By 6 days there was substantial recovery, apparently as a result of repopulation of the thymic epithelium by host stem cells. This was confirmed by transplanting thymus fragments between individuals of op-

posite sexes. Karyotype analysis showed that the thymus contained lymphocytes of the sex of the recipient. However, karyotype analysis of lymphoma cells taken from recipient line-6 chickens that had received thymus grafts from line-7 birds of the opposite sex showed that, in the majority of cases, the lymphomas consisted of cells of donor origin. It is concluded that the susceptibility of line-7 chickens is largely attributable to the greater susceptibility of their T-lymphocytes to infection and transformation by Marek's disease virus, and that this susceptibility can be transferred to genetically resistant line-6 birds by adoptive transfer of the cells in the form of thymus fragments. (Author abstract) (16 Refs)

EXPERIMENTAL STUDIES: RNA TUMOR VIRUSES

43. SPECIFIC DIFFERENTIATION EVENTS INDUCED BY ERYTHROPOIETIN IN CELLS INFECTED IN VITRO WITH THE ANEMIA STRAIN OF FRIEND VIRUS.

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Proc Natl Acad Sci USA; 79(2):635-639 1982

Mouse bone marrow cells infected in vitro with the anemia strain of Friend leukemia virus form large clusters (bursts) of erythroblasts after 5 days in culture in methylcellulose medium. Two types of erythroblast populations can be isolated from bursts of infected cells by manipulation of the culture conditions. One type of erythroblast, which is obtained when erythropoietin (EP) is added to the culture, has proliferated and undergoes differentiation to become an erythrocyte. The second type of erythroblast, which is obtained when no EP is added to the culture, is the product of extensive proliferation, but it fails to undergo the terminal stages of erythroblast differentiation. Comparisons of these two types of erythroblasts demonstrate that specific EP effects include changes in the nucleus, cytoplasm, and membrane of the treated cells. Those events of erythroid differentiation shown to be directed by EP were extrusion of the nucleus from the erythroblast, induction of uroporphyrinogen I synthetase activity, increased iron incorporation into protoporphyrin, synthesis of alpha- and beta-globin polypeptides due largely to increased mRNA production, and synthesis and incorporation of spectrin into the cell membrane. In this system, EP promotes these effects without observable stimulation of progenitor proliferation in addition to that caused by the virus alone. Thus, the role of EP in terminal erythrocyte differentiation is not simply that of an erythroid-specific mitogen. (Author abstract) (30 Refs)

44. EFFECT OF BENZO[A]PYRENE ON FRIEND VIRUS LEUKEMOGENESIS, CFU-S VIABILITY, AND INDUCTION OF HUMORAL IMMUNITY.

Raikow RB, OKunewick JP, Buffo MJ, Jones DL
Cancer Res. Lab., Allegheny-Singer Res. Corp., Allegheny General Hosp., Pittsburgh, PA, 15212
Experientia; 38(1):126-127 1982

The compound benzo[a]pyrene (BP) potentiated the induction of leukemia by low doses of Friend virus in SJL/J mice if injected 2 days before the virus. BP also reduced the viability of hematopoietic stem cells (CFU-S) within this time interval but had little effect on the induction of humoral immunity (the PFC response). (Author abstract) (18 Refs)

45. GENETIC MAPPING OF ECOTROPIC MURINE LEUKEMIA VIRUS-INDUCING LOCI IN SIX INBRED STRAINS.

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J Exp Med; 155(2):524-534 1982

Mendelian segregation analysis was used to map chromosomal genes for the induction of endogenous N- and B-tropic ecotropic retroviruses (V loci) in high and low leukemic mouse strains. Segregation analysis resulted in the genetic mapping of V loci in six inbred strains to five mouse chromosomes. The V locus of A/J was mapped to chromosome 5 and shown to be allelic with that of BALB/cJ and C3H/HeJ (Cv); this suggests that Cv represents a stable ancestral V locus present in Bagg albino stocks before separation of inbred lines. The single, poorly inducible V locus of C57BL/10J and one of the four high virus loci of C58/Lw were mapped to the same region of chromosome 8 and may present an allelic pair with different patterns of expression. An N-tropic V locus of the SEA/GnJ mouse was mapped to chromosome 9, and one of the three V loci of C3H/FgLw was mapped to chromosome 7. The endogenous B-tropic virus of B10.BR/SgLi was mapped to chromosome 11. Several of the endogenous proviral sequences appear to be closely linked with cellular genes involved with sensitivity or resistance to retroviral infection or affecting lymphoid differentiation. Identification and separation of individual V loci aids in their characterization and makes it possible to identify DNA fragments carrying biologically defined proviruses. (26 Refs)

46. GENETIC CONTROL OF SENSITIVITY TO MOLONEY LEUKEMIA VIRUS IN MICE: V. ROLE OF H-2-LINKED GENES IN THE CONTROL OF ANTI-FMR CYTOLYTIC T-LYMPHOCYTES.

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Cell Immunol; 65(2):317-324 1981

Three H-2-linked genes, Rmv1, Rmv2, and Rmv3 control the resistance of mice against Moloney virus (MLV)-induced leukemias. It has been shown previously that they function as immune response (Ir) genes regulating the level of antivirus antibodies. In the present experiments, the cell-mediated antitumor response has been studied in a series of inbred strains selected for their resistance or sensitivity to the MLV-induced disease. We failed to detect any relationship between resistance and sensitivity and the ability to produce cytolytic T lymphocytes (CTL) directed against the virus-induced FMR cell surface antigen. Furthermore, the role of each Rmv gene has been studied separately using congenic pairs of mice differing at only one of these loci: we failed to evidence any influence of these genes in the cell-mediated antitumor reactions as measured by the ability to lyse syngeneic FMR(+) target cells. Nevertheless a gene mapping in the D region of the MHC but probably different from RMv3 controls the response of a subset of anti-FMR CTL restricted by the H-2Kk antigens, with higher response in H-2Dd animals than in H-2Db animals. This observation confirms the existence of H-2D region associated Ir genes regulating the CTL-mediated antitumor immune responses by choosing the subset of responder CTL, and suggests that a fourth H-2-linked gene plays some role in the genetic control of the anti-FMR immune response. (Author abstract) (15 Refs)

47. MOLONEY MURINE LEUKEMIA VIRUS-INDUCED TUMORS: RECOMBINANT PROVIRUSES IN ACTIVE CHROMATIN REGIONS.

van der Putten H, Quint W, Verma IM, Berns A
Departement de Biologie Animale, Laboratoire de Differenciation Cellulaire, 154, Route de Malagnou, CH-1224, Chene-Bougeries, Geneve, Switzerland
Nucleic Acids Res; 10(2):577-592 1982

The DNase I sensitivity of chromosomal DNA regions carrying integrated proviral genomes of Moloney (M-MuLV) and AKR Murine Leukemia Virus (AKR-MuLV), and the cellular homologue of the mos-gene (c-mos) of Moloney Sarcoma Virus (MSV) were studied in tumor tissues of leukemic mice. The genetically transmitted sequences of M-MuLV, AKR-MuLV, and the c-mos gene are all in DNase I resistant chromatin conformations in M-MuLV-induced tumors. Each M-MuLV-induced tumor contained at least one somatically acquired integrated recombinant MuLV genome that displayed two main characteristic features of active chromatin; (a) a configuration hypersensitive to DNase I, and (b) extensive hypomethylation. DNase I hypersensitive sites were mapped at the junction of cellular sequences and the 5'-viral large terminal repeat (LTR). Expression of a recombinant MuLV seems therefore to be a necessary feature to maintain the transformed state. (Author abstract) (28 Refs)

48. CHARACTERIZATION OF GENOME STRUCTURE OF AMPHOTROPIC AND ECOTROPIC WILD MOUSE RETROVIRUSES.

Lai MM, Shimizu CS, Rasheed S, Pal BK, Gardner MB
Dept. Microbiology, Univ. Southern California Sch. Medicine, Los Angeles, CA, 90033
J Virol; 41(2):605-614 1982

We studied the RNA genomes of several wild mouse Type C retroviruses by using RN ase T1-oligonucleotide fingerprinting. The amphotropic and ecotropic viruses of field strain 1504 produced very similar oligonucleotide fingerprints, but each also had several unique oligonucleotides. All of these unique oligonucleotides were located in the env gene region and were probably responsible for the host range differences between these viruses, as well as the lymphomagenic and paralytogenic properties of the viruses. We obtained similar results with the amphotropic and ecotropic viruses of another field strain (4070), which was isolated from a mouse from a different trapping area. The amphotropic viruses of several field strains (strains 1504, 4070, and 1313) were more closely related than the ecotropic viruses of different strains (strains 1504, 4070, and 4996). These findings suggested that the genetic sequences of the amphotropic viruses are more conserved than those of ecotropic viruses isolated from the same wild mice. (Author abstract) (26 Refs)

49. CHARACTERIZATION OF XENOTROPIC AND DUAL-TROPIC TYPE C RETROVIRUSES ISOLATED FROM ABELSON TUMOUR.

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J Gen Virol; 58(part1):115-125 1982

Tumors induced in Balb/c mice by Abelson virus complex were found to contain a xenotropic virus (A-X-MuLV) and an NB-tropic, dual-tropic virus (NBX), in addition to the Moloney leukemia virus (M-MuLV) and the defective, transforming Abelson virus genome. Both A-X-MuLV and NBX virus were presumably present in a genomically masked form and could be recovered only by co-cultivation of tumor cells with permissive cells. Only about 0.87% and 0.13% of the viruses in the co-culture supernatant represented A-X-MuLV and NBX virus respectively; the majority were M-MuLV. The NBX virus acted more efficiently than the HIX virus as helper to rescue murine sarcoma virus (MSV) from S+L- cells of hamster, rat and mouse origin, whereas the converse was true for those of cat and human origin. The interference and neutralization patterns suggested that the NBX virus was an env gene recombinant between A-X-MuLV and M-MuLV. The fact that NBX virus cross-reacted in radioimmunoassays with gp70s of both M-MuLV and Balb:virus-2 provides evidence for the recombinant nature of the NBX gp70-coding gene which was probably derived from both M-MuLV and a virus similar to Balb:virus-2 or A-X-MuLV. The presence of a unique antigenic determinant on the gp70 of NBX virus is also suggested. Both A-X-MuLV and NBX virus cross-reacted with type-specific p12s of M-MuLV and Balb;virus-2, suggesting that the gag gene coding for p12 of NBX virus was derived from the A-X-MuLV, which was itself a recombinant, its p12-coding gene being derived from both Balb:virus-2-like virus and M-MuLV. The NBX virus was not oncogenic when tested in newborn Balb/c mice. (Author abstract) (40 Refs)

50. THE SAME GENETIC LOCUS DIRECTS DIFFERENTIATION-LINKED EXPRESSION OF ENDOGENOUS RETROVIRUS GP70 ON THYMOCYTES AND SPLEEN CELLS IN THE MOUSE.

Tung JS, Shen FW, Viamontes G, Palladino M, Fleissner E
Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York, NY, 10021
Immunogenetics; 15(1):103-108 1982

Expression of the major envelope glycoprotein (gp70) of murine leukemia virus (MuLV) was studied in spleen cells of C57BL/6 (B6) and 129 mice that are negative for thymocytes surface antigen (GIX) and spleen cells of their congeneic GIX+ and GIX- derivatives. Proteins with a mol wt of approx 70,000 daltons were specifically recognized by a group-specific anti-gp70 serum in spleen cell lysates of 129, B6, and B6-GIX+ mice; 129-GIX- cells were negative. A monoclonal antibody specific for GIX+ MuLV gp70 precipitated the same gp70 molecules on spleen cells from the GIX+ strains. Occurrence of spleen cell gp70 in these strains appeared to controlled by the same genetic locus (Gv-1) that determines the presence of GIX+ gp70 on thymocytes. The presence of gp70 on spleen cells from B6-nu mice as well as on cytotoxic spleen T cells indicated that gp70 molecules are expressed by both T and non-T cells. (15 Refs)

51. INHIBITION OF THE RELEASE OF VIRION-ASSOCIATED MURINE LEUKEMIA VIRUS GENOMIC RNA BY VESICULAR STOMATITIS VIRUS.

Chan JC, Mohr MD, Knesek JE, Bowen JM, East JL
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Intervirology; 16(3):191-200 1981

The genomic RNAs of murine leukemia virus (MuLV) and vesicular stomatitis virus (VSV) were distinguishable based on a difference in sedimentation coefficient, polyadenylic acid content, and nucleotide sequence homology. Applying these biochemical characteristics, we found that the release of virion-associated MuLV genomic RNA from virus-producing cells was inhibited by VSV as early as 2 hr after superinfection.

This finding offers an explanation to our previous inability to detect MuLV (VSV) pseudotype formation during mixed infection with VSV and MuLV. (Author abstract) (39 Refs)

52. DIFFERENT T-CELL SUBTYPES ARE ASSOCIATED WITH PATHOLOGICALLY DISTINCT FORMS OF MOLONEY LEUKEMIA VIRUS (M-MULV)-INDUCED LYMPHOMA.

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Dept. Tumor Biology, Karolinska Institutet, S 104 01 Stockholm, Sweden
Int J Cancer; 29(2):163-167 1982

The T-cell enzyme markers, terminal deoxy-nucleotidyl transferase (TdT) and 20 alpha hydroxysteroid dehydrogenase (20 alpha SDH), were used to classify lymphomas induced by the Moloney leukemia virus (M-MuLV). Different subtypes of T cells were shown to be involved in different types of lymphoma. Thymomas were TdT-positive and grew as sc solid tumors at the site of inoculation. Spleen cell s from mice with generalized lymphoma were of two types. In the majority of cases the lymphomas consisted of 20 alpha SDH-positive cells that homed to spleen and lymph nodes upon transplantation. In a few cases the cells of enlarged spleens were TdT-positive and, like the TdT-positive thymomas, could be transplanted as sc tumors. Thus, TdT-positive and 20 alpha SDH-positive T-cell lymphomas can be distinguished by their homing properties. Preleukemic thymus cells from M-MuLV inoculated mice can, after transfer to 400-R irradiated syngeneic hosts, induce new lymphomas by virus release or grow in an autonomous fashion in the recipients. Whether of donor or recipient type, these lymphomas are TdT-positive. In contrast, preleukemic bone marrow cells give lymphomas of donor type which are as heterogeneous for T-cell enzymes as are lymphomas induced by neonatal inoculation of M-MuLV. (Author abstract) (14 Refs)

53. IN VITRO STUDIES OF THE MECHANISM OF LEUKEMOGENESIS. II. CHARACTERIZATION OF ENDOGENOUS MURINE LEUKEMIA VIRUSES ISOLATED FROM AKR THYMIC EPITHELIAL RETICULUM CELL LINES.

Yanagihara K, Hamada K, Seyama T, Imamura N, Yokoro K
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J Virol; 41(2):360-366 1982

Thymic epithelial reticulum (TER) cell lines were established from thymuses of a young healthy AKR mouse (A2T), a preleukemic AKR mouse (A6T), and two lymphoma-bearing AKR/Ms mice (ASLT-1 and ASLT-2). Numerous Type-C virus particles with occasional budding forms were observed in all cell lines. Expression of XC-detectable, N-tropic, ecotropic virus was observed in every cell line, whereas the presence of xenotropic and mink cell focus-inducing (MCF) viruses could be detected only in TER cells derived from preleukemic and leukemic mice. Expression of xenotropic virus in various cells of newborn and young AKR mice could readily be induced by IUdR treatment, whereas MCF virus was never detected in these cells, with the exception of the A2T cell line after more than 20 passages, in which MCF virus with dual-tropic infectivity emerged in addition to ecotropic and xenotropic viruses. These spontaneous and induced MCF viruses were purified, and their virological properties were characterized. The cloned MCF viruses (MCFs AT1, AT2, AT3, and AT4-IU) showed dual tropism and produced cytopathic effect-like foci in mink lung cells. Preinfection with either ecotropic or xenotropic virus interfered with the infectivity of MCF viruses. Spontaneous leukemogenesis in AKR mice was accelerated by the inoculation of MCF viruses. These findings indicate that TER cells could serve as the host cells for the genetic recombination of the endogenous MuLV; the recombinant MuLV, MCF virus, appears to be most closely associated with leukemogenesis in AKR mice. (Author abstract) (2 9 Refs)

54. CHARACTERIZATION OF PROVIRUSES CLONED FROM MINK CELL FOCUS-FORMING VIRUS-INFECTED CELLULAR DNA.

Khan AS, Repaske R, Garon CF, Chan HW, Rowe WP, Martin MA
Lab. Molecular Microbiology, Natl. Inst. Allergy and Infectious Diseases, Bethesda, MD, 20205
J Virol; 41(2):435-448 1982

Two proviruses were cloned from EcoRI-digested DNA extracted from mink cells chronically infected with AKR mink cell focus-forming (MCF) 247 murine leukemia virus (MuLV), using a lambda phage host vector system. One cloned MuLV DNA fragment (designated MCF 1) contained sequences extending 6.8 kilobases from an EcoRI restriction site in the 5' long terminal repeat (LTR) to an EcoRI site located in the envelope (env) region and was indistinguishable by restriction endonuclease mapping for 5.1 kilobases (except for the EcoRI site in the LTR) from the 5' end of AKR ecotropic proviral DNA. The DNA segment extending from 5.1 to 6.8 kilobases contained several restriction sites that were not present in the AKR ecotropic provirus. A 0.5-kilobase DNA segment located at the 3' end of MCF 1 DNA contained sequences which hybridized to a xenotropic env-specific DNA probe but not to labeled ecotropic env-specific DNA. This dual character of MCF 1 proviral DNA was also confirmed by analyzing heteroduplex molecules by electron microscopy. The second cloned proviral DNA (designated MCF 2) was a 6.9-kilobase EcoRI DNA fragment which contained LTR sequences at each end and a 2.0-kilobase deletion encompassing most of the env region. The MCF 2 proviral DNA proved to be a useful reagent for detecting LTRs electron microscopically due to the presence of nonoverlapping, terminally located LTR sequences which effected its circularization with DNAs containing homologous LTR sequences. Nucleotide sequence analysis demonstrated the presence of a 104-base-pair direct repeat in the LTR of MCF 2 DNA. In contrast only a single copy of the reiterated component of the direct repeat was present in MCF 1 DNA. (Author abstract) (44 Refs)

55. STUDIES OF CAUSAL CORRELATIONS AND PATHOGENESIS OF LEUKOSIS, NEPHROBLASTOMAS, OVARIAN TUMORS, AND OSTEOPETROSIS AFTER INFECTION WITH AVIAN LEUKOSIS VIRUSES.

Loliger HC, Von dem Hagen D, Hartmann W
Institut fur Kleintierzucht, D-3100 Celle, W. Germany
DTW; 89(1):22-28 1982

Correlations between infection with avian leukosis viruses and appearance of leukosis (LK), nephroblastomas (NB), ovarian tumors (OT), and osteopetrosis were studied. Several lines of chickens with varying viral sensitivities were infected with avian myeloblastosis virus (AMV), avian erythroblastosis virus (AEV), or Marek herpes virus (MHV). Pathological conditions developed in chickens susceptible to A- or B-group avian leukosis viruses (ALV) but not in resistant chickens. Pleiomorphic diseases deve loped in chickens infected with AMV but not in chickens infected with MHV or AEV. MHV induced only monomorphic lymphoreticular neoplasias; induction was inde-

pendent of the stage of genetic susceptibility. The incidence of pathological conditions decreased as the age of chickens at the time of infection increased. In older chickens leukemia appeared only as acute, early stages of disease. Occurrence of leukemia was related to the concentration of virus introduced. Nephroblastomas and cystadenomas appeared as late effects of viral infection and increased in frequency as the frequency of acute leukemia decreased. Osteopetrosis developed in all lines susceptible to AMV, particularly in dysgammaglobulinemic lines. No association of nephrogenic or osteogenic tumor factor with viruses of subgroup A or B was demonstrated. Results indicate that the targets of AMV are pluripotential embryo-reticular cells and undifferentiated hemoblast present only in newly hatched chicks, and that the viruses act by blocking cellular differentiation. (25 Refs) (In GER)

56. ISOLATION OF AN ANTIGEN FOR DIAGNOSIS OF ENZOOTIC CATTLE LEUKEMIA USING AGAR GEL IMMUNODIFFUSION TECHNIC.

Mateva V
Central Res. Veterinary Inst., Sofia, Bulgaria
Vet Med Nauki; 18(4):45-46 1981

A method of isolation of cattle leukemia virus antigen is described. The virus was isolated from the culture medium or from the cells of fetal lamb kidney infected with cattle leukemia virus. The antigen formed a precipitation band with the leukemic sera. Activity and specificity of precipitation band did not differ from that produced by glucoprotein antigens. The antigen was effectively used for the diagnosis of enzootic cattle leukemia. (no Refs) (In BUL)

REVIEWS AND OTHER RELATED STUDIES

57. FUNCTION OF THE RETROVIRUS LONG TERMINAL REPEAT.

Temin HM
McArdle Lab., Univ. Wisconsin, Madison, WI, 53706
Cell; 28(1):3-5 1982

The long terminal repeat (LTR), a series of nucleotides derived from the 5' and 3' ends of viral RNA and located at the end of all infectious retrovirus DNA, is described. Information obtained from studies of the morphological transformation of NIH/3T3 cells after treatment with DNA containing LTR sequences and cellular homologs of viral transforming genes (oncogenes) is presented. Other data about LTR has been obtained from recombination of LTR from mouse mammary tumor virus with coding sequences. The presence of LTR has been used to explain differences in leukemogenicity of recombinant avian leukosis viruses. Evidence for the role of the ends of the LTR in processes related to integration is described. The LTR appears to contain most of the sequences involved in making retroviruses autonomous replicating elements. The relationship among viral, cellular, and LTR DNA is considered. (no Refs)

58. NEW HUMAN PAPOVAVIRIDAE VIRUSES.

Shevliagin VIa
N. F. Gamaleia Inst. Epidemiology and Microbiology, Moscow, USSR
Usp Sovrem Biol; 92(3):338-353 1981

Isolation, physico-chemical, antigenic, and biological properties of new viruses from Papovaviridae family are reviewed. In addition to simian virus SV-40, Papovaviridae group includes BK virus isolated from the urine of a patient subjected to kidney transplantation, and JCV virus isolated from a patient with Hodgkin's disease complicated by progressive multifocal encephalopathy. BK virus was shown to induce sarcomas, ependymomas and insulinomas in Syrian hamsters; the incidence and latent period depended upon the route of administration and the degree of virus purification. BK virus failed to induce tumors in rabbits, guinea pigs, young rats, and monkeys. JCV virus showed replication only in the glial cells of human embryo. The intracranial or sc inoculation with JCV virus produced malignant gliomas and pineocytomas in Syrian hamsters. Peripheral neuroblastomas with metastases to the liver, bone marrow, and lymph nodes were observed after intraocular infection with JCV virus. (140 Refs) (In RUS)

59. HUMAN CANCERS AND HUMAN VIRUSES.

Waterson AP
Royal Postgraduate Medical Sch., London W12 0HS, England
Br Med J; 284(6314):446-448 1982

The connection between human cancers and human viruses is reviewed. Evidence of malignancies attributable to DNA viruses, similar to those of animals, is growing. A type of human leukemia retrovirus, the human T-cell leukemia virus, has been isolated. Hepatitis B virus has been shown to be of primary hepatocellular carcinoma and Epstein-Barr virus the cause of Burkitt's lymphoma and nasopharyngeal carcinoma; cytomegalovirus may be implicated in Kaposi's sarcoma and human papillomaviruses may cause skin cancer. To be implicated in oncogenesis, a virus should be found in tumor cells and be capable of transforming normal cells of the same species in vitro and inducing tumors in studies with animals. Human T-cell leukemia virus has been shown to be infectious when cultivated with human umbilical cord leukocytes, transforming them into virus-producing lines. Epstein-Barr virus causes disease only rarely on primary infection in childhood, but in adolescence or adult life it gives rise to infectious mononucleosis. Hepatitis caused by hepatitis B virus can be followed by chronic active hepatitis and cirrhosis and is a suspected cause of primary hepatocellular carcinoma. Malignant change has been reported in laryngeal papillomas, in genital warts, and in epidermodysplasia verruciformis. Factors other than viruses which influence malignant transformation are the genetic constitution and immune state of the patient. The virus-cell relation is not simple. (29 Refs)

60. THE NATURE OF CHROMOSOME BANDS AND THEIR SIGNIFICANCE FOR CANCER RESEARCH.

Sumner AT
Clinical and Population Cytogenetics Unit, Western General Hosp., Edinburgh EH4 2XU, Scotland
Anticancer Res; 1(4):205-215 1981

Chromosome bands are discussed with respect to classification, properties, banding techniques, and their significance to cancer research. The two main classes of chromosome bands are constant, heterochromatic bands (CHB) and fluctuant bands (FB), with kinetochores and nucleolar organizers recognized as separate classes. CHB have been associated with regions containing satellite DNA in many species. FB correspond to pachytene chromomeres, and may represent the condensation process occurring in mitotic chromosomes. Banding patterns are used to identify whole or parts of chromosomes, gene mapping, and to study the clinical significance of polymorphisms of CHB. Banding techniques revealed the presence of the Philadelphia chromosome in most cases of chronic mye-

loid leukemia; few, if any, other cancers show such a clear correlation with a specific chromosomal abnormality. Banding techniques have revealed that cancers tend to be associated with particular chromosome abnormalities and that certain chromosomes tend to be altered in cancerous cells. Burkitt's lymphoma retinoblastoma, and Wilm's tumor are each associated with specific chromosome abnormalities. The presence of 'homogenously staining regions' and double minute chromosomes in some tumor cells is discussed. While chromosome changes in cancer cells can be identified by banding techniques, the significance of such changes is unclear. (131 Refs)

61. PROCANCER CLASS OF GENES AND GENERATION OF CHROMOSOME MUTATION.

Sasaki MS, Ejima Y
Radiation Biology Center, Kyoto Univ., Yoshida-konecho, Sakyo-ku, Kyoto 606, Japan
Gann Monogr Cancer Res; 27:85-94 1982

The nature of inherent mutation associated with chromosome instability and high cancer risks is discussed. Human genetic syndromes associated with chromosome instability include Fanconi's anemia (FA), ataxia telangiectasia (AT), Bloom's syndrome (BS), incontinentia pigmenti (IP), and, perhaps xeroderma pigmentosum (XP). Chromosome aberrations are primarily of the chromatid type, indicating that the chromosome mutations in these diseases arise in connection with DNA replication. FA, AT, and IP have a significantly high frequency of chromosome aberrations, while the other diseases show normal aberration rates. DNA damage left unrepaired in AT and FA cells might not be subject to repair by post-replication error-prone repair mechanisms or such a mechanism might not operate in these cells. Genetically-determined cancer proneness appears to be caused by an intrinsic sensitivity of instability to chromosome mutation; gross chromosomal change is a prime importance in mutation toward cancer. Certain types of procancer genes with dominant traits express a mutator function and promote chromosome recombination in their somatic cells. Such mutations of de novo origin occur in familial polyposis coli, Gardner's syndrome, Peutz-Jegher's syndrome, nevoid basal cell carcinoid syndrome, hereditary retinoblastoma, dominantly-inherited familial leukemia, and familial colon cancer. The nature of germinal mutations responsible for organ-specific cancer proneness is discussed. (37 Refs)

62. PATHOLOGICAL EFFECTS OF LOW DOSES. LOW LINEAR TRANSFER ENERGY RAYS.

Dousset M
7, rue de la Gruerie, F 9190 Gif-sur Yvette, France
J Radiol; 62(11):556-560 1981

Somatic and genetic effects of low doses of low linear transfer energy are discussed in view of the diagnostic and therapeutic use of radiation. Prospective and retrospective studies relating radiation dose and effects are described. Findings on individuals exposed to irradiation at Hiroshima and Nagasaki are presented. With low dose radiation, there appears to be a curvilinear relationship between dose and effect with no threshold phenomenon. In experimental animals, irradiation prior to nidation results in the loss of the fertilized egg due to lack of implantation. During the first 35 days of human pregnancy, irradiation can result in malformations in the embryo. Fetal exposure to irradiation has been shown to increase the incidence of malignant disease. Radiation doses of greater than 100 rads can cause growth retardation among children irradiated prior to age 6 yr. An increased incidence of thyroid cancer has been observed among children less than 10 yr old exposed to low dose radiation. Adult exposure to radiation has been related to leukemia and cancers of the breast, thyroid, respiratory tract, bone, and digestive tract. Genetic effects of radiation are discussed. Male germ cells seem to be more sensitive to radiation than those of females. Germinal cells show varying sensitivities to radiation. (28 Refs) (In FRE)

63. ARSENIC-STATE OF THE ART.

Landrigan PJ
Div. Surveillance, Hazard Evaluations, and Field Studies, NIOSH, 4676 Columbia Parkway, Cincinnati, OH, 45226
Am J Ind Med; 2(1):5-14 1981

Occupational and domestic exposure to arsenic in United States of America is briefly reviewed: human elimination mechanisms; assay implications; acute poisoning; subacute and chronic toxicity to the skin (dermatitis, Bowen's disease, basal cell and squamous cell carcinomas), liver (cirrhosis, angiosarcoma), respiratory tract (lung cancer), and nervous (peripheral neuropathy), cardiovascular (acrocyanosis), 'blackfoot disease' (gangrene), myocardial infarction, Reynaud's (phenomenon), and hematopoietic (disturbed erythropoiesis, equivocal cancer) systems. Animal cancer-induction studies remain negative. Mutagenicity/chromosomal aberration studies in bacterial-animal-human systems are touched upon. (50 Refs)

64. INTERPRETING CLUES TO CHILDHOOD CANCER.

Napolitano LV, D'Angio GJ, Grosfeld JL, Mauer AM, Miller DR, Sinks LF, Peterson RD
No affiliation given
Patient Care; 16(3):19-21,23,24,30,32,35,38,39,42,43,45,46,48-50,55 63 1982

Clues, evaluation, and epidemiology of pediatric cancer are discussed. Of the familial or congenital conditions associated with an increased risk of malignancy, the condition with the highest risk (leukemia in 1%) is Down's syndrome. Pediatric malignancies often mimic other diseases. Cancer is a possible diagnosis in a child with epistaxis, easy bruising, gingival swelling or bleeding, or signs and symptoms of a CNS disorder or an apparent infectious disease. The symptoms of a solid tumor depend on tumor site. Abdominal tumors are often silent until they interfere with normal function. The physician should carefully question the parent who brings the child in. Even if clinical examination is negative, the parent knows the child better than the physician and is more alert to subtle signs of illness. Children with aniridia should be examined for possible Wilms' tumor every 3-6 mo during the first 2-3 yr of life. However, repeated hematologic examinations are not indicated for children at high risk of leukemia, because the differential WBC may be entirely normal in a child who only 2 mo later has obvious leukemia. Needle biopsy is usually contraindicated for abdominal or thoracic masses. Lymphadenopathy in children is more likely to be caused by an infectious disease than by a malignancy. If the enlarged nodes are hard, do not regress in response to a course of antibiotics, and (sometimes) increase in size over a 2-mo period, the possibility of Hodgkin's disease or non-Hodgkin's lymphoma should be considered and a lymph node biopsy performed. The biopsy specimen should be prepared for all basic studies (electron microscopy, histochemical analysis, fresh tissue analysis, cell surface markers, a touch prep slide). A step-by-step approach to diagnosis of the 11 most common pediatric malignancies is presented. (3 Refs)

65. INFECTIOUS MONONUCLEOSIS.

Dorchy H
Departement Universitaire de Pediatrie, Hopital Saint-Pierre, Bruxelles, Belgium
Rev Med Brux; 2(10):977-985 1981

The etiology, physiopathology, and oncogenicity of Epstein Barr virus and the diagnosis, treatment, and prevention of EBV-induced infectious mononucleosis (IM) are discussed. EBV specifically infects B-lymphocytes and also nasopharyngeal epithelial cells. In vivo or in vitro, EBV can inactivate lymphocytes and provoke their lymphoblastic transformation to establish a continuous line of lymphoid cells. Carcinogenic properties of EBV include its ability to produce lymphoblastic transformation, to integrate its viral genome into host cell, and the persistance of a latent infection. EBV is associated with two mali gnant tumors: Burkitt's lymphoma (BL) and nasopharyngeal cancer (NPC). BL occurs mainly in children 2-14 yr, attacks the maxilla preferentially but may also involve the abdomen or lymph nodes, and results from the uncontrolled division of a clone of B lymphocytes containing EBV genome. In EBV-related NPC, epithelial cells carry the EBV genome. Genetic and environmental risk factors for NPC are described. Topics discussed in relation to IM include the following: epidemiology, clinical signs (polyadenopathies, angina, splenomegaly, hepatomegaly, edema, and skin eruptions), rare manifestations of EBV infections, complementary examinations, development, and prognosis. (48 Refs) (In FRE)

66. POLYCYTHAEMIA.

Goldstone AH
Univ. Coll. Hosp., London, England
Practitioner; 226(1363):72-76 1982

Polycythemia vera (PV), one of the spectrum of myeloproliferative disorders, is often associated with myelofibrosis and thrombocythemia. Overlapping features of these diseases and transitions from one to another often occur. These transitions seem to represent the neoplastic proliferation of a myeloid stem cell capable of producing red cells, platelets, and granulocytes. Splenomegaly and pruritus are characteristic of PV rather than secondary (reactive) polycythemia. Secondary polycythemia may be caused by an erythropoietin-producing tumor (eg, kidney, ovarian, or bronchial), a disease causing hypoxia (including heart or lung disease, acclimatization to high altitudes, stress, etc), or an abnormal Hb. The differential diagnosis of PV and secondary polycythemia often depends on the exclusion of any secondary cause. In both PV and secondary polycythemia, the major causes of death are thrombotic and hemorrhagic conditions. About 25% of PV patients develop acute leukemia, typically myeloid and refractory to therapy. Treatment directed at controlled the packed cell vol can increase the median survival time in PV patients from 2 yr to 13-14 yr. Venesection is the treatment of choice for reducing the hematocrit rapidly. The systemic treatments most often used are P32 (3-8 mCi, iv, every 6-12 mo according to the platelet count; max cumulative dose, 35 mCi) and intermittent busulfan (2-6 mg/day). Whether or not these treatments increase the risk of leukemic transformation is not clear. The leukemic phase may represent the natural progression of the disease. (no Refs)

* U. S. GOVERNMENT PRINTING OFFICE : 1982—361-847/121

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NOTICE OF CURRENT REVIEWS: CARCINOGENESIS

As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

CHEMICAL CARCINOGENESIS

1. AN EVALUATION OF THE GENETIC TOXICITY OF EPICHLORHYDRIN. A REPORT OF AN EXPERT GROUP OF THE INTERNATIONAL COMMISSION FOR PROTECTION AGAINST ENVIRONMENTAL MUTAGENS AND CARCINOGENS.
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Mutat Res; 87(3):299-319 1981

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3. CHEMICAL CARCINOGENESIS AND SMOKING.
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Can J Public Health; 72(6):381-385 1981

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4. CELLULAR TRANSFORMATION BY RADIATION: INDUCTION, PROMOTION, AND INHIBITION.
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DIETARY FACTORS IN CARCINOGENESIS

6. BETA-CARBOLINES, PSYCHOACTIVE COMPOUNDS IN THE MAMMALIAN BODY.
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17. ONCOGENESIS BY RNA TUMOR VIRUSES.
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Muller R, Rajewsky MF
(c/o Rajewsky) Institut fur Zellbiologie (Tumorforschung), Universitat Essen (GH), Hufelandstrasse 55, Essen 1, W. Germany
J Cancer Res Clin Oncol; 102(2):99-113 1981

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Takemura N
Dept. Public Health, Jikei Univ., 25-8, Nishi-Shimbashi 2-chome, Minato-ku, Tokyo, 105, Japan
Sangyo Igaku; 23(4):355-365 1981
In JPN

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Levine L
Dept. Biochemistry, Brandeis Univ., Waltham, MA, 02254
Adv Cancer Res; 35:49-79 1981

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Scalabrino G, Ferioli ME
Inst. General Pathology, Univ. Milan, 20133 Milan, Italy
Adv Cancer Res; 35:151-268 1981

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EPIDEMIOLOGY AND ETIOLOGY OF HUMAN LYMPHORETICULAR MALIGNANCIES: VIRAL STUDIES

1. NATURAL ANTIBODIES TO THE STRUCTURAL CORE PROTEIN (P24) OF THE HUMAN T-CELL LEUKEMIA (LYMPHOMA) RETROVIRUS FOUND IN SERA OF LEUKEMIA PATIENTS IN JAPAN.

Kalyanaraman VS, Sarngadharan MG, Nakao Y, Ito Y, Aoki T, Gallo RC
(c/o Gallo) Lab Tumor Cell Biology, NCI, NIH, Bethesda, MD, 20205
Proc Natl Acad Sci USA; 79(5):1653-1657 1982

We investigated the involvement (in adult T-cell leukemias and lymphomas) of the human T-cell leukemia virus (HTLV) that was previously isolated in one of our laboratories from cultured T cells of some patients in the United States with leukemias and lymphomas involving relatively mature T cells. High titers of antibodies capable of quantitative precipitation of 125I-labeled p24, a well characterized core protein of HTLV, were detected in 12 of 12 patients with untreated adult T-cell leukemia (ATL). (1 negative was a patient on chemotherapy). Ten of the 12 positive samples were from an area where the disease is endemic. Strong precipitating antibodies were also detected in five of seven cases of T-cell malignant lymphoma (TML) which differs from ATL by having fewer leukemic cells in the peripheral blood. High antibody titers were also observed in one of five cases of acute monoblastic leukemia and one of eight cases of chronic myelogenous leukemia in the blast phase of the disease. Low to moderate titers of antibodies were detected in several categories of leukemia (2 cases of blast-phase chronic myelogenous leukemia, 2 cases of acute lymphoblastic leukemia of the null-cell type, and 1 case of acute myelogenous leukemia). Among all categories of leukemias, except ATL and TML, more cases were negative than positive for anti-p24 activity. All of 79 sera from normal Japanese, including 39 collected from the endemic ATL area of southwest Japan, were negative for antibodies to HTLV p24. All the positive reactivities observed were highly specific to HTLV. The only competition observed in the precipitation of HTLV p24 was with HTLV or with cell lines expressing HTLV and not with various animal retroviruses or a large number of human and subhuman primate cell lines, not known to be producing HTLV. The data strongly indicate an association of HTLV with the increased incidence of ATL in parts of Japan, probably with other forms of leukemias in Japan, and, less commonly, with certain T-cell malignancies in the United States. (26 Refs)

2. ADULT T-CELL LYMPHOMA-LEUKAEMIA IN BLACKS FROM THE WEST INDIES.

Catovsky D, Rose M, Goolden AW, White JM, Bourikas G, Brownell AI, Blattner WA, Greaves MF, Galton DA, McCluskey DR, Lampert I, Ireland R, Bridges JM, Gallo RC
Medical Res. Council Leukaemia Unit, Royal Postgraduate Medical Sch., London, England
Lancet; 1(8273):639-642 1982

Six Black patients (5 born in the West Indies and 1 in Guyana), aged 21-55 yr, had adult T-cell lymphoma-leukemia diagnosed in the UK. This disorder is rare in Europe and the USA, but is more common in Japan. Five patients had severe hypercalcemia which correlated with disease activity, although osteolytic lesions were found in only one. Other clinical features were lymphadenopathy and a high white blood-cell count (range 27-67 x 10(9)/l) with a predominance of pleomorphic lymphoid cells with pronounced nuclear irregularities prominent at ultrastructural level. The cells in all cases formed rosettes with sheep red blood-cells and lacked terminal transferase. Analysis with OKT monoclonal antibodies in four cases confirmed a mature T-cell phenotype defined as helper/inducer (T4+, T6-, T8-) in three. Combination chemotherapy resulted in short-lived remissions; four patients died and two have survived 3-6 mo. The disease in these patients is indistinguishable on clinical and pathological grounds from adult T-cell leukemia/lymphoma in Japan. Geographical clustering among certain racial groups suggests common etiological factors in the pathogenesis of this disease. The finding of high titer antibody against the structural core protein (p24) of a new human C-type leukemia virus (human T-cell leukemia/lymphoma virus) in all tested cases from this series and data from all but one case from Japan suggest that one such factor may be viral. (Author abstract) (no Refs)

3. SEARCH FOR RETROVIRUS EXPRESSION IN MEN - FAILURE TO DEMONSTRATE RETROVIRUS-SPECIFIC ANTIGENS IN NORMAL AND MALIGNANT TISSUE.

Micheel B, Wunderlich V, Hertling I
Zentralinstitut fur Krebsforschung, Lindenberger Weg 70/80, DDR-1115 Berlin-Buch, E. Germany
Arch Geschwulstforsch; 52(3):169-173 1982

Immunological experiments using the Sepharose bead immunofluorescence assay to demonstrate retrovirus antigens in different human tissues are presented. With some of the extracts (in particular from placentas and leukemic tissues) slightly positive reactions were observed, especially in the interspecies-specific type C virus assay. An unequivocally positive result could not be obtained in any case. With some samples, the test was negative when repeated, with others the values were just at the significance border and turned out to be insignificant when the competition by uninfected cellular extracts was taken as a reference. Results indicated that a virus specificity was nonexistent. (17 Refs)

EPIDEMIOLOGY AND ETIOLOGY OF HUMAN LYMPHORETICULAR MALIGNANCIES: OTHER STUDIES

4. FAMILIAL MULTIPLE MYELOMA. A REVIEW OF THIRTY-SEVEN FAMILIES.

Shoenfeld Y, Shaklai M, Berliner S, Gallant LA, Pinkhas J
Dept. Medicine 'D', Tel Aviv Univ. Sackler Sch. Medicine, Beilinson Medical Center, 49100 Petah Tiqva, Israel
Postgrad Med J; 58(675):12-16 1982

The review of the pertinent literature disclosed 36 reports of familial multiple myeloma, described mostly in siblings, to which the authors add one more family. These patients did not differ significantly form those with non-familial myeloma with regard to sex, age, distribution of monoclonal proteins, clinical and laboratory data, and the course and prognosis of the disease. An increased incidence of immunoglobulin abnormalities was observed in healthy relatives of patients affected with famili al myeloma. In most cases the time interval of the diagnosis of myeloma in a family member of a known patient was under 4 yr. These observations, in conjunction with reports of myeloma occurring in clusters in a community and the appearance of myeloma in spouses raise the possibility of an environmental factor (virus?) which may contribute to the pathogene-

sis of myeloma in genetically predisposed individuals. Multiple myeloma should be added to the list of neoplastic diseases in which the family history is relevant and in which genetic and possibly environmental factors may be pathogenetically involved. (Author abstract) (49 Refs)

5. EPIDEMIOLOGIC CHARACTERISTICS OF CHILDHOOD CANCER.

Austin DF, Nelson VE, Johnson LF
Resource for Cancer Epidemiology, Health Services, 1450 Broadway, Oakland, CA, 94612
Front Radiat Ther Oncol; 16:9-17 1982

In the San Francisco metropolitan area, the incidence of malignancies in childhood (0-19 yr old) remained substantially unchanged over a 10-yr period (1969-1978), but the mortality rate declined substantially in all pediatric age groups. The mortality/incidence ratio in all age groups combined declined by about 20% during this time, apparently reflecting improved treatment procedures. These changes have been greater in children 0-14 yr old than in the 15-19 age group. Examination of mean annual age-specific mortality rates for the leukemias suggests that leukemias (especially acute leukemias) of childhood and adulthood may be etiologically different diseases. There responses to treatment suggest that they may be biologically different diseases. Possible etiologic factors for childhood leukemia include prenatal radiation exposure, chromosomal abnormalities, and possibly antigenic stimulation of the WBC population at a critical period of gestation by certain biologic agents. The children of women who had been in the first trimester of pregnancy during an influenza A epidemic showed a 3-4-fold increase in the risk of childhood leukemia. Investigations of childhood leukemia clusters have almost uniformly been inconclusive. A cluster of Ewing's sarcoma (30 recorded cases over an 8-yr period; 20% of the entire 8-yr incidence) has been discovered in one small community (within a 30-block diameter) in the San Francisco area. It is hoped that investigations of such clusters may provide clues for the prevention of the disease. (6 Refs)

6. LONG-TERM EFFECTS OF AZATHIOPRINE IN RHEUMATOID ARTHRITIS.

Urowitz MB, Smythe HA, Able T, Norman CS, Travis C
Rheumatic Disease Unit, Wellesley Hosp., 160 Wellesley St. E., Toronto, Ontario, M4Y 1J3, Canada
Ann Rheum Dis; 41(Suppl1):18-22 1982

Potential early signs of malignancy were assessed in 36 patients (8 men, 28 women; mean age 57.8 yr) receiving azathioprine (APR: mean, 1.08 mg/kg/day x 38.5 mo) for rheumatoid arth ritis and 49 controls (13 men, 36 women; mean age 51.4 yr) not receiving APR. The mean duration of arthritis was somewhat longer in the APR group (15.3 vs 11.9 yr). The groups were comparable in their symptomatic status, chest x-rays, and most laboratory test results. As compared to the controls, the APR groups showed significantly lower WBC counts, a higher frequency of megaloblastic features in the bone marrow, lower serum folate levels, and a higher frequency of chromosomal aberrations in the bone marrow. Malignancies had occurred in first-degree relatives of 15/36 APR-treated patients and 6/49 controls. The APR and control groups showed comparable frequencies of inflammatory or fibrotic pulmonary abnormalities (15/36 vs 9/49), benign breast masses (1/28 vs 3/36 women), and abnormal urine cytology (4/36 vs 1/49) with no evidence of cancer on follow-up. Neoplasms were observed in 7/36 APR patients (3/7 were malignant or potentially malignant tumors) and 5/49 controls (1/5 was a malignant tumor); the difference in incidence rates were not significant. The only non-Hodgkin's lymphoma observed in the group was in a control patient. In the APR group, the tumors developed after a mean of 1.6 yr of APR therapy. Three APR-treated patients with cancer had positive family histories of cancer; none of the controls with tumors had family histories of cancer. Elevated titers of alpha-fetoprotein or carcinoembryonic antigen were observed in some of the APR group (1/36 and 7/25 patients tested, respectively; none of these patients had a detectable cancer) and none of the controls. Further studies in larger groups of APR-treated patients and longer treatment periods are recommended. (53 Refs)

7. COFFEE, TEA AND CANCER: HOW TO TEST HYPOTHESES ON LIFESTYLE AND DISEASE?.

Olsson H, Brandt L
Onkologiska kliniken, Lund, Sweden
Lakartidningen; 79(4):196-197 1982

Coffee and tea consumption of 550 tumor patients was analyzed based on questionnaire data. The patients included 19 with seminomas, 36 with cancer of the upper part of the digestive tract (lips, oral cavity, epipharynx, hypopharynx and esophagus), 59 with Hodgkin's disease, 64 with tumors of the larynx and lungs, 36 with thyroid tumors, 120 with cancer of the urinary bladder or kidneys, 28 with skin cancer, 94 with breast cancer, 16 with testicular teratomas, 28 with melanomas, 20 with cancer of the lower parts of the digestive tract (stomach, bile ducts, pancreas, colon and rectum), and 18 with tumors of the paranasal sinuses, auditory meatus and parotid glands. The median coffee consumption of the patients was 3-5 cups/day, ie, approx the same as in the general population. Fifty-three per cent of the patients with seminomas, 50% of those with cancer of the upper part of the digestive tract and 47% of those with Hodgkin's disease consumed large amounts of coffee (5 cups/day or more). The median tea consumption of the patients was 0 cup/day. Forty-four per cent of the patients with testicular teratomas, 31% of those with thyroid tumors, 32% of those with seminomas, and 29% of those with Hodgkin's disease consumed large amounts of tea (2 cups/day or more). The findings indicate that hypotheses based on complex data on lifestyle (education, occupational status, living conditions, dietary and smoking habits, and alcohol consumption) should be tested in epidemiological studies, rather than the possible relationship between tea and coffee consumption, on one hand, and certain diseases, on the other hand. (6 Refs) (In SWE)

CYTOGENETIC AND MORPHOLOGIC STUDIES

8. KARYOTYPICALLY DISTINCT SUBPOPULATIONS IN ACUTE LEUKEMIA WITH SPECIFIC GROWTH REQUIREMENTS.

Lowenberg B, Hagemeijer A, Swart K
Inst. Hematology, Erasmus Univ., P. O. Box 1738, Rotterdam, The Netherlands
Blood; 59(3):641-645 1982

Bone marrow and blood cells of a patient with acute monoblastic leukemia with subclones marked with specific karyotypic abnormalities were investigated. In order to more precisely evaluate the proliferative abilities of these populations, leuke-

mic cell enriched fractions were prepared and incubated in two colony assays. Colony forming cells of the disparate clones had growth advantages in different systems which shows that their proliferation depended on the presence of selective stimulatory factors in culture. In one assay, at diagnosis, colonies from the minor clone were demonstrated exclusively. It is suggested that the assays measured distinct cellular stages of myeloid differentiation and the findings indicate that prior to diagnosis the neoplasm had evolved into subsets with progressive dedifferentiation. Differences of growth in vitro correlated with the different roles of these clones in the clinical history of the disease. Approaches based on differential cloning of tumor stem cells as in this example, may be useful for discriminating biological properties of heterogeneous subpopulations within neoplasms, and may facilitate the cytogenetic recognition of minimal clones among composite malignant cell specimens. (Author abstract) (25 Refs)

9. BIBLIOGRAPHIC REVIEW AND OUR PERSONAL EXPERIENCE IN CYTOGENETIC STUDIES IN CHRONIC MYELOID LEUKEMIA.

Brieux de Salum S, Labal de Vinuesa M
Departamento de Cultivo de Tejidos y Citogenetica, Instituto de, Investigaciones Academia Nacional de Medicina, Buenos Aires, Argentina
Medicina (B Aires); 41(Suppl):170-178 1981

Chronic myeloid leukemia (CML) and the chromosomal anomaly Philadelphia chromosome 1 (Ph1) were discussed. Patients with CML had 77.5% Ph1 positive and 22.5% had Ph1 negative (-). The patients with Ph1-consisted usually of older men with low platelet, low WBC and shorter survival. Therapy for the patients with CML was also discussed. (46 Refs) (In SPA)

10. PROGNOSTIC SIGNIFICANCE OF CYTOGENETICAL STUDIES IN CHRONIC GRANULOCYTIC LEUKAEMIA.

Cervantes F, Rozman C, Ballestra F, Mila M
Postgraduate Sch. Hematology, Casanova 143, Barcelona-36, Spain
Scand J Haematol; 28(1):77-81 1982

In a series of 121 patients with chronic granulocytic leukemia (CGL) the frequence and prognostic significance of two cytogenetical features (absence of Ph'-chromosome and presence of Ph'-mosaicism) were studied. Thirteen percent of the patients were Ph'-negative, these patients showing a shorter survival than the Ph'-positive ones (p less than 0.005). Twenty three instances of Ph'-mosaicism were found (22.5%). This feature was observed either at diagnosis or after treatment, and irrespective of the patient's being in chronic or blastic phase of CGL, but in no case later than 2 yr from diagnosis of the disease. Ph'-mosaicism patients vs the remainder of the Ph'-positive group were compared for survival, and no difference was found. The lack of prognostic significance of Ph'-mosaicism was evident regardless of the latter feature being detected at diagnosis or after treatment. (Author abstract) (15 Refs)

11. CLONES WITH 3 PH1 AND 4 PH1 IN THE TERMINAL PHASE OF THREE CASES OF CHRONIC MYELOID LEUKEMIA.

Cabrol C, Peytremann R, Maurice PA
Univ. Inst. Medical Genetics, 8, chemin Thury, CH-1206 Geneva, Switzerland
Acta Haematol (Basel); 67(3):150-159 1982

G-banded cytogenetic studies of three male patients in the terminal phase of chronic myeloid leukemia showed the following abnormalities: in the first case, the presence of a medullar cell line with 51 chromosomes and 3 Ph1; in the second case, a clone with 65 chromosomes and 4 Ph1, and in the third patient a clone with 53 chromosomes and 3 Ph1. In all three cases, G-banding revealed the Ph1 translocation to be of the usual type: t(9;22) (q34;q11) and there was discordance between the number of Ph1 and 9q+. There was no obvious correlation between the presence of mutliple Ph1 and the clinical or cytological features. These three cases were detected as part of a recent G-banded cytogenetic survey of nine individuals in the blastic phase studied by the authors. The frequency of multiple Ph1 observed in this sample of blastic-phase leukemia is unusually elevated, raising the question of the origin of such a high incidence. (Author abstract) (12 Refs)

12. CYTOGENETIC STUDIES ON ERYTHROPOIETIC AND MYELOPOIETIC PROGENITOR CELLS IN VITRO IN CHRONIC MYELOGENOUS LEUKEMIA.

Grilli G, Carbonell F, Fliedner TM
Abteilung fur Klinische Physiologie und Arbeitsmedizin, Universitat Ulm, Oberer Eselsberg M 24, 7900 Ulm (Donau), W. Germany
Haematologica (Pavia); 66(6):733-739 1981

Cytogenetic studies on erythropoietic (EP) and myelopoietic (MP) progenitor cells in vitro were performed using bone marrow and/or peripheral blood from seven patients with chronic myeloid leukemia [four were in chronic phase (CP) and three in blast phase (BP)]. Mononuclear cells from peripheral blood were grown in vitro 12-14 days in the presence of erythropoietin using the methylcellulose technique. Colcemid was introduced and 2 hr later colonies were aspirated. Of the three patients in BP no erythroid colony growth was noticed; all blood metaphases (29/29, 3/3, 50/50) as well as all myeloid colony-forming units in culture (CFU-C: 7/7, 3/3, 8/8) studied had Philadelphia 1 chromosome (Ph 1). Bone marrow of the 3/4 patients in CP had Ph 1 in 18/18, 30/30, and 36/36 of the metaphases; blood of the 4/4 patients in CP had Ph 1 in 33/33, 50/50, 13/13, and 23/24 of the metaphases; myeloid CFU-C of the 2/4 patients in CP had Ph 1 in 5/5 and 4/6 of the metaphases, and erythroid burst-forming units of the 3/4 patients in CP had Ph 1 in 12/12, 9/10 and 10/10 of the metaphases. Also, other cytogenetic abnormalities besides Ph 1 were seen. One patient in CP had cells with normal karyotype derived from myeloid and erythroid progenitors (4/6 and 9/10). Coexistence of normal and leukemic clones was discussed. (19 Refs) (In ITA)

13. MOSAICISM T(9; 22)/T(1; 9; 22) RESULTING IN THE PHILADELPHIA CHROMOSOME.

Berger R, Bernheim A, Bussel A
Laboratoire de Cytogenetique UER d'Hematologie, Hopital Saint-Louis, 2, place du Dr-Fournier, F-75475 Paris, France
Nouv Rev Fr Hematol; 23(4):209-212 1981

The chromosomes of a 76-yr-old man with chronic myelocytic leukemia (CML) were analyzed. Bone marrow studies revealed the usual t(9; 22) translocation in addition to a secondary t(1;9; 22) translocation which resulted from a complex rearrangement of three chromosomes. The importance of correlating clinical findings and karyotypic data from patients with CML is stressed. (9 Refs) (In FRE)

14. TRANSLOCATION (9;11)(P21;Q23) IN THREE CASES OF ACUTE MONOBLASTIC LEUKEMIA.

Hagemeijer A, Hahlen K, Sizoo W, Abels J

Dept. Cell Biology and Genetics, Erasmus Univ., P.O. Box 1738, 3000 DR Rotterdam, The Netherlands

Cancer Genet Cytogenet; 5(2):95-105 1982

A balanced translocation t(9;11)(p21;q23) was found in three cases of acute monoblastic leukemia (AMol or M5 according to the FAB classification). This translocation, which involves small chromosomal segments of approx the same length, is difficult to recognize with certainty when techniques other than R-bands are used. A new specific association is proposed between this translocation and acute leukemia of the M5 type. (Author abstract) (23 Refs)

15. T(15;17) TRANSLOCATION IN ACUTE PROMYELOCYTIC LEUKEMIA (M3) AND CYTOLOGICAL 'M3-VARIANT'.

Berger R, Bernheim A, Daniel MT, Valensi F, Flandrin G

Laboratoire de Cytogenetique, Institut de Recherches sur les Leucemies, et les M aladies du Sang Hopital Saint-Louis, 2, place du Dr A-Fournier, F-75475 Paris Cedex 10, France

Nouv Rev Fr Hematol; 23(1):27-38 1981

Of 158 patients with nonlymphoblastic acute leukemia, 20 exhibited the t(15;17) chromosomal translocation. Of these 20 patients, 15 had M3-type acute promyelocytic leukemia (APL); 5 had the chromosomal translocation but did not fit normal cytological criteria for APL (M3-variant: M3var). Patients with M3 APL showed leukopenia or moderate hyperleukocytosis. Patients with M3var had marked hyperleukocytosis. Bone marrow aspirates from M3 patients were characterized by highly granular blast cells with irregular nuclei. 'Faggot cells' containing Auer bodies were found in varying numbers. Some patients had cells with small, single- or bi-lobed nuclei, suggesting different degrees of maturation among blast cells. Blast cells from M3var patients, particularly cells from peripheral blood, were more faintly granular and generally large. Nuclei were irregular and cytoplasm was abundant. The general hematologic picture was similar to acute monocytic leukemia. One M3var patient had cytological characteristics intermediate between the other M3var patients and the M3 patients. M3 cells showed a positive chloroacetate esterase reaction; M3var cells were negative. Results suggest differences in maturation and kinetics of blast cells in M3 and M3var APL. (27 Refs)

16. THREE CASES OF ACUTE PROMYELOCYTIC LEUKEMIA. EXHIBITION OF THE T(15; 17) TRANSLOCATION IN THE THREE CASES.

Fraisse J, Jaubert J, Vasselon C, Brizard C

Laboratoire de Cytogenetique et Service Central d'Hematologie, Centre Hospitalier Regional Universitaire, F-42023 Saint-Etienne, France

Nouv Rev Fr Hematol; 23(3):163-164 1981

In three patients with acute promyelocytic leukemia, cytogenetic studies performed on bone marrow aspirate revealed a chromosome abnormality translocation t(15; 17) in most of the mitoses that were examined. The breakage points were identical in the three cases and were localized in the area of the 15q25 and 17q22 bands. The chromosome preparations were obtained after a 48 hr culture. (9 Refs) (In FRE)

17. CYTOGENETIC STUDIES IN PRELEUKEMIC STATES.

Larripa I, Brieux de Salum S

Departamento de Tejidos y Citogenetica, Instituto de Investigaciones, Hematologicas Academia Nacional de Medicina, Buenos Aires, Argentina

Medicina (B Aires); 41(Suppl):179-186 1981

Chromosomal studies were evaluated for diagnosis and especially for prognosis of preleukemic states. Patients without previous treatment and without clinical or hematologic symptoms of leukemia included 20 patients with refractory anemia (RA), 7 with sideroblastic anemia (AS), 21 with polycythemia vera (PV). Ten patients with ferropenic anemia served as controls, because they have normal karyotypes. Of th e 21 patients with PV, all had numerical cytogenetic alterations (CA) and in 17 they were associated with structural alterations (SA), but 15 were in good condition and 5 were stationary. Seven patients with AS had numerical CA; in two they were associated with SA; one of them with 7q developped acute myeloblastic leukemia (AML), the other was stationary, while five were in good condition. Of the 20 patients with the RA, 4 had polyploidy, 3 had diffuse chromosomes (DC), the rest had numerical CA associated in two of them with SA. The two patients with RA died without developping leukemia, one with DC and the other with CA associated with SA (r and 2q +). Four or the patients with RA developped AML, four were in poor condition, one was stationary, and nine were in good condition. Anomalous clones in cytopenic states indicate bad prognosis (high risk for leukemia or short survival), but they are not indicating for PV. (42 Refs) (In SPA)

18. CYTOGENETIC STUDIES USING HPCM-STIMULATED SHORT-TERM LIQUID CULTURES OF CIRCULATING HEMOPOIETIC PRECURSOR CELLS IN PATIENTS WITH MYELOFIBROSIS.

Ganser A, Carbonell F

Abteilung fur Klinische Physiologie und Arbeitsmedizin, Universitat Ulm, Oberer Eselsberg, D-7900 Ulm (Donau), W. Germany

Blut; 44(2):111-114 1982

Cytogenetic studies were performed on nine patients (5 men, 40-62 yr old and 4 women, 54-70 yr old) with myelofibrosis. Two men and one woman showed signs and symptoms of acute leukemia. Mononuclear cells were separated from samples of peripheral blood and cultured in medium conditioned with fresh human placenta (HPCM). Metaphase preparations were made after 2 days of incubation. Two patients showed evidence of chromosomal abnormalities. All metaphases in cell cultures from one patient with acute myeloid leukemia showed the loss of the Y chromosome. Cell cultures from a patient not showing signs of leukemia showed an abnormal stem line with alterations of chromosomes 7 and 9 (46,XX,7q-,-9,+mar). Results indicate that culturing of hematopoietic cells in HPCM is suitable for determining whether myeloproliferative syndromes are the result of autochthonous proliferation and differentiation of stromal cells or of irreversible abnormalities of hematopoietic stem cells. Detection of abnormal clones indicates that myelofibrosis is a secondary effect of a neoplastic disorder. Absence of abnormal clones does not, however, rule out a leukemic process. (16 Refs)

19. ABNORMALITIES OF CHROMOSOME NO. 17 IN MYELOPROLIFERATIVE DISORDERS.

Borgstrom GH, Vuopio P, De la Chapelle A
Dept. Medical Genetics, Univ. Helsinki, Haartmaninkatu 3, 00290 Helsinki 29, Finland
Cancer Genet Cytogenet; 5(2):123-135 1982

In routine analyses, abnormalities of chromosome Number 17 were found in the bone marrow cells of 28 patients with Ph(1)-positive and 3 patients with Ph(1)-negative chronic myeloid leukemia (CML), 4 patients with acute nonlymphocytic leukemia (ANLL), and 4 patients with preleukemia. With three exceptions, all patients were in the blastic (CML) or the terminal phase. In 28 patients, the aberrant chromosome Number 17 arose by clonal evolution from the karyotype found at diagnosis or before the terminal phase. The abnormalities encountered were an isochromosome for the long arm, i(17q), (26 cases), translocations involving Number 17 (12 cases), trisomy 17 (3 cases), and ring 17 (1 case). In 35 patients, there was an unbalanced structural aberration of at least one of the Number 17 chromosomes. In every case (35/35), detailed analysis of the structurally abnormal Number 17 revealed loss of the distal part of the short arm (or possibly most of the short arm). Gain of the long arm (or at least its proximal part) was also common, but not invariably present (26/35). It is suggested that loss of 17p is a highly nonrandom event related to blastic crisis in CML and the terminal phase in other myeloid leukemias. (Author abstract) (26 Refs)

20. GIANT MARKER CHROMOSOME IN FANCONI'S ANEMIA TRANSFORMING INTO ERYTHROLEUKEMIA IN AN ADULT.

Rotzak R, Kaplinsky N, Chaki R, Blei F, Berkowitz M, Goldman B, Frankl O
Dept. Medicine, Chaim Sheba Medical Center, Tel-Hashomer, Israel
Acta Haematol (Basel); 67(3):214-216 1982

A 22-yr-old patient diagnosed as having Fanconi's aplastic anemia turning to acute erythroleukemia is described. The diagnosis was based on congenital malformations, pancytopenia and the known chromosomal abnormalities. We call attention to the patient's age at time of diagnosis, the turn into erythroleukemia, the cataracts and the giant marker chromosome in bone marrow cells - features that make this patient exceptional. (Author abstract) (10 Refs)

21. AN ANALYSIS OF CHROMOSOME FINDINGS IN NON-HODGKIN'S LYMPHOMAS.

Kaneko Y, Abe R, Sampi K, Sakurai M
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Cancer Genet Cytogenet; 5(2):107-121 1982

Banding studies were done on tissues from tumors excised from 22 Japanese patients with non-Hodgkin's lymphomas. All tumors were found to be associated with aneuploidy. The chromosome abnormalities were diverse, with each chromosome type being involved in these abnormalities. Terminal deletions, derivative chromosomes as a result of unbalanced or non-reciprocal translocations, and markers of totally or partially unknown origin accounted for the majority of the structural abnormalities. Balanced reciprocal translocations were seen only occasionally. The 14q+, 6q-, partial trisomy of 1q, 11q+, 18q+, and 19q+ abnormalities were seen in more than two patients. The incidence of a missing sex chromosome was significantly higher than that of autosomes, but no particular other karyotypic abnormality seemed to be associate d with the event. All six patients whose chromosomes could be totally characterized were in complete remission. Patients with one or more markers of unknown origin (either totally or partially), had a median survival of only 8 mo (p less than 0.01). Five of the former six patients showed a nodular histology. Fifteen of the latter 16 patients had a diffuse histology, with 13 of the 15 having diffuse histiocytic lymphoma. The median survival of 9.5 mo for the 14 with only abnormal metaphases in the lymphatic tissues (AA-group) was shorter than the 26+ mo for the 7 patients with both normal and abnormal metaphases (AN-group). Thus certain aspects of chromosomal changes appear to correlate with histology and/or prognosis in non-Hodgkin's lymphomas. (Author abstract) (29 Refs)

22. CYTOGENETIC STUDIES ON FOUR CASES OF NON-ENDEMIC BURKITT LYMPHOMA.

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Inst. Human Genetics, Sarphatistraat 217, 1019 BX Amsterdam, The Netherlands
Med Pediatr Oncol; 10(1):71-84 1982

Cytogenetic studies carried out on four children with non-endemic Burkitt lymphoma showed: (1) Two with the typical translocation t(8;14) (q24;1q32); (2) one with a variant t(2;8)(p11;24); and (3) one with apparently normal chromosomes 8 and 14. Additional chromosomal variation was present in all four patients. Two were shown to have a duplication of part of the long arm of chromosome 1 (1q23 to 1q32 and 1q23 to 1q42). Epstein Barr virus studies on two patients showed that one was positive and the other negative. A comparison of these results with other non-endemic cases in the literature has been made revealing a wider range of chromosomal variation than has been hitherto reported for endemic cases. The finding that chromosome 8 is also involved in the variant translocations in Burkitt lymphoma suggests that its changes may contribute more to the tumor development than the 14q+. (Author abstract) (40 Refs)

23. VARIANT CHROMOSOMAL T(8;22) TRANSLOCATION IN FOUR FRENCH CASES WITH BURKITT LYMPHOMA-LEUKEMIA.

Berger R, Bernheim A, Bertrand S, Fraisse J, Frocrain C, Tanzer J, Lenoir G
Laboratoire de Cytogenetique, Institut de Recherches sur les Leucemies, et les Maladies du Sang Hopital Saint-Louis, 2, place du Docteur Alfred-Fournier, F-75475 Paris Cedex 10, France
Nouv Rev Fr Hematol; 23(1):39-41 1981

A variant chromosomal translocation is reported in four French patients with Burkitt's lymphoma (BL). Three cases were not associated with Epstein-Barr virus. Cytogenetic studies showed three clones in two cases and one primary clone in one case. A t(8;22) translocation was found in all four cases; the translocation is apparently not unusual. Examination of rearrangements in chromosome 8 is urged in study of BL. (14 Refs)

BIOCHEMICAL, IMMUNOLOGICAL AND OTHER CELL BIOLOGY STUDIES

24. LEUKEMIC-LIKE MEMBRANE PROPERTIES ACQUIRED BY B LYMPHOCYTES WHEN DEPLETED OF 185,000-DALTON MACROMOLECULAR INSOLUBLE COLD GLOBULIN.

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Blood; 59(3):555-562 1982

Human peripheral blood lymphocytes can be phenotypically identified by the presence of one or both of two proteins, 225,000-dalton macromolecular insoluble cold globulin (225-MICG) and 185,000-dalton MICG (185-MICG). T cells synthesize and insert into their plasma membrane 225-MICG, null cells 185-MICG, and B cells both 225 and 185-MICG. In contrast, the monoclonal B cells of chronic lymphocytic leukemia are characterized by the presence of 225-MICG and the absence of 185-MICG. We have recently found it possible to chemically deplete 185-MICG from viable normal B cells by treating them with diisopropylfluorophosphate (DFP), thus making normal B cells phenotypically resemble leukemic cells. In the present report we determined whether certain peculiar properties of these leukemic cells would be associated with the normal B cells chemically depleted of 185-MICG. In normal B cells, SIg diffuses in the lipid bilayer to form clusters and caps under appropriate conditions, while in chronic lymphocytic leukemia (CLL) cells this does not occur. Normal B cells depleted of 185-MICG fail to undergo capping of SIg or surface MICG under appropriate conditions. Both DFP-treated B cells and CLL cells tend to rupture when smeared on a glass slide. Both CLL cells and DFP-treated B cells fail to secrete 225-MICG after it has been synthesized intracellularly. The relationship of these findings to the mechanisms of secretion and capping are discussed. (Author abstract) (42 Refs)

25. MEMBRANE-BOUND AND CELLULAR IMMUNOGLOBULINS IN HUMAN B-LYMPHOMA LINES AND DERIVED HYBRIDS.

Spira G, Aman P, Silvian I, Koide N, Ber R, Klein G
Faculty Medicine, Technion, P.O.B. 9649, Haifa, 31096, Israel
Immunobiology; 160(3/4):340-351 1981

Hybrids derived from the fusion of cell lines representing different maturation stages were studied for their membrane and cellular immunoglobulin expression. The hybrids can be subdivided into three groups, with one common parental line in each group. In the first group, Raji cells represent the common parent: it contains small amounts of membrane and cytoplasmic mu and kappa chains. In the second group, PUT is the common parent, an ouabain and TG-resistant subline of the BL-derived P3HR-1 line. PUT contains a truncated intracellular mu chain. The third group consists of hybrids between K562, an EBV-negative human erythroleukemia line and two different BL lines. Membrane-immunoglobulin expression was intermediate between the parental lines in the first two groups derived from the fusion of two BL lines. In the third group, hybridization with the K562 cell suppressed the membrane-Ig expression of the B-cell partner. Total cellular immunoglobulin determinations showed that some cells synthesized light chains in excess of heavy chains, others contained an excess of heavy chains, while still others had equal amounts of heavy and light chains. The hybrids showed a variety of patterns, including amplification of the parental phenotypes, appearance of new phenotypic combinations, and eclipse of one or both parental phenotypes. A comparison of the total and the membrane-associated immunoglobulin patterns suggests independent handling of intracellular and membrane immunoglobulin synthesis. (Author abstract) (28 Refs)

26. PLASMA FUCOSYLTRANSFERASE AS AN INDICATOR OF IMMINENT BLASTIC CRISIS.

Shah-Reddy I, Kessel DH, Chou T, Mirchandani I, Khilanani U
Section Hematology, Hutzel Hosp., 4707 St. Antione, Detroit, MI, 48201
Am J Hematol; 12(1):29-37 1982

Plasma fucosyltransferase activity was evaluated as an indicator of an impending blastic transformation in 25 patients with chronic granulocytic leukemia (CGL). Fifteen age- and sex-matched controls were also studied. The level of enzyme activity was significantly higher in the plasma of patients with blastic transformation (1,630 +-570 units) compared with steady state chronic granulocytic leukemia (509 +-110 units) and normal controls (354 +-57 units). In three patients with CGL, a rise in fucosyltransferase activity preceded any other clinical or laboratory parameter of blastic transformation by 16-20 wk. (Author abstract) (22 Refs)

27. NONPOLAR LIPID METHYLATION - IDENTIFICATION OF NONPOLAR METHYLATED PRODUCTS SYNTHESIZED BY RAT BASOPHILIC LEUKEMIA CELLS, RETINA AND PAROTID.

Kloog Y, Zatz M, Rivnay B, Dudley PA, Markey SP
Lab. Clinical Science, Natl. Inst. Mental Health, Bethesda, MD, 20205
Biochem Pharmacol; 31(5):753-759 1982

Incorporation of radioactivity from [3H- or 14C-methyl]methionine into nonpolar lipids has been investigated in rat basophilic leukemia (RBL) cells, retina and rat parotid gland. These nonpolar methylated lipids were extracted into heptane and characterized by thin-layer chromatography, high performance liquid chromatography, gas chromatography, and mass spectrometry. The major methylated nonpolar lipid product in the RBL cells themselves was ubiquinone-9, which accounted for about 90% of the nonpolar lipid and 20-30% of the total radioactive lipid formed. There was a modest increase in the methylation of nonpolar lipids upon stimulation of the RBL cells with IgE and anti-IgE, but the significance of this change is uncertain. In contrast to whole cells, RBL membrane fractions (incubated with [3H-methyl]-S-adenosylmethionine) incorporated radioactivity primarily into fatty acid methyl esters and not ubiquinone. A third product, 2-(methylthio)-benzothiazole, was formed by RBL cells, retina and minced parotid upon incubation in enriched media. This product was formed enzymatically, apparently by the known enzyme S-thiomethyltransferase, using the thiol substrate which contaminates these media. Evidence suggests that the enzyme may reside, at least in part, on the surface of the cells. (Author abstract) (37 Refs)

28. QUANTITATION OF RNA-DEPENDENT PLATELET DNA POLYMERASE IN PATIENTS WITH MYELOPROLIFERATIVE DISORDERS.

Strayer DR, Brodsky I, Caranfa MJ, Gillespie DH
Dept. Hematology Medical Oncology, Hahnemann Medical Coll. and Hosp., 230 North Broad St., Philadelphia, PA, 19102
Br J Haematol; 50(3):521-530 1982

Platelets from 28 patients with the myeloproliferative diseases (MPD) polycythemia vera (9), essential thrombocythemia (6), myelofibrosis with myeloid metaplasia (5) and chronic myelogenous leukemia (8) were examined for an RNA-dependent DNA polymerase activity using standardized conditions permitting highly reproducible quantitation. Low levels of activity were detected in platelets of normal individuals, but platelets of nearly all MPD patients (25/28) possessed higher levels. The polymerase activity correlated with diagnosis ($p = 0.001$) and did not correlate with platelet counts (p greater than 0.2). Quantitation of this RNA-dependent DNA polymerase activity may be a useful parameter in the diagnosis of myeloproliferative disorders. (Author abstract) (20 Refs)

29. IN VITRO CELLULAR IMMUNE REACTIVITY OF SOLUBLE ANTIGENS OBTAINED FROM CULTURED LEUKEMIC CELLS IN CHRONIC MYELOID LEUKEMIA.

Khare AG, Advani SH, Gangal SG
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Indian J Exp Biol; 19(6):524-527 1981

The preparation of potent antigenic substances from leukemia cells by culturing in vitro for various time periods was investigated. Antigens prepared from uncultured cells produced significant inhibition of leukocyte migration in 9/11 tests. Leukemic cells cultured for 24 hr yielded antigens with very high lymphocyte transformation activity in 7/11 tests. Chronic myeloid leukemia leukocyte/lymphocyte samples tested with cells cultured for 48 and 72 hr showed a progressive reduction in the number of positive reactions. Leukemic cell antigens prepared after 24 hr of incubation showed greater activity than antigens prepared from uncultured cells. (16 Refs)

30. IDENTIFICATION AND PARTIAL CHARACTERIZATION OF SPECIFIC ANTIGEN ON ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN.

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Dept. Pediatrics, Mie Univ. Sch. Medicine, Tsu, Japan
Mie Med J; 31(1):57-65 1981

Identification and partial physical and chemical characterization of tumor-specific antigen (TSA) associated with acute lymphoblastic leukemia (ALL) are reported. Peripheral blood samples w ere obtained from patients with clinically and cytologically diagnosed ALL upon admission to the hospital. Cells were classified as T cell, B cell, or non-T non-B ALL. Also studied were Molt-4B (T cell ALL) and Raji (B cell ALL) cell lines. Rabbit antisera were raised against ALL cells and purified. In indirect immunofluorescence tests, the rabbit antisera reacted with 34/37 non-T non-B samples, 1/4 T cell samples, and no B cell, acute myeloblastic leukemia, chronic lymphoblastic leukemia, chronic myeloblastic leukemia, or Molt-4B samples. The antisera did not react with fetal thymocytes, fetal bone marrow, cord blood, neuroblastoma cells, or normal bone marrow cells. TSA from leukemic cells was extracted by the 3 M-KCl method. In immunoprecipitation tests antiserum reacted with a component of mol wt of 80,000-90,000 daltons. Extracts from non-ALL cells did not react with antisera. The isoelectric point of the TSA was pH 4-5. Results indicate that non-T non-B and a limited number o T cell ALL have a TSA of mol wt 80,000-90,000 daltons. (18 Refs)

31. SURFACE MARKERS IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA.

Liang DC, Hsieh KH, Lin KS
Dept. Clinical Pathology, Coll. Medicine, Natl. Taiwan Univ., Taipei, Taiwan, Republic of China
Taiwan I Hsueh Hui Tsa Chih; 80(11):1160-1168 1981

Sixty-one childhood acute lymphoblastic leukemia (ALL) patients were studied, and the correlation between the immunological classifications and clinical features was explored. Patients with more than 85% of lymphoblasts (LB) in their peripheral blood and/or bone marrow were included in the study. Patients received chemotherapy, and after complete remission most received craniospinal irradiation. Two patients with 85% LB were negative for erythrocyte (E) and erythrocyte antibody complement (EAC) surface markers. Among the other 45 patients with bone marrow checked, 6 were E+ALL, 1 was EAC+ALL, and 38 were E-, EAC-ALL. Among nine early cases of ALL, eight were E-, EAC-ALL. For the deceased six patients with E-, EAC- surface markers, the survival was 18-84 mo (mean 45 mo, median 44.5 mo). Among 36 patients entered later (EL) into the study, 6 were E+ALL and 30 E-, EAC-ALL. The initial clinical features of EL patients are shown. Comparison of 6 E+ and 30 E-, EAC- cases, respectively, showed that median age of onset was 10 and 6 yr, male to female ratio was 5:1 and 14:16, white counts greater than 20 x 10(3) cubic mm in the former and less than 20 x 10(3) cubic mm in the latter, and 4 mediastinal involvements in the E+ group compared with 1 in the E-, EAC-group. Actuarial curves of EL are presented. The E+ group had higher mortality rate (66.6%) and shorter duration of survival (median 7.0 mo, mean 9.0 mo) than the E-, EAC-group. Results indicate that ALL ia a heterogeneous disease with respect to clinical characteristics and prognosis. (39 Refs)

32. BENCE JONES PROTEINS: MALIGNANT OR BENIGN?

Solomon A
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N Engl J Med; 306(10):605-607 1982

Whether benign monoclonal gammopathies are truly benign or presage the eventual development of a plasma-cell/lymphocytic neoplasm or amyloidosis is discussed. The transition from benign to malignant gammopathy has been reported in patients with monoclonal serum immunoglobulins. At least 60-80% of patients with multiple myeloma have Bence Jones proteinuria; in approx 20% of patients, Bence Jones proteins (BJP) may be the sole monoclonal immunoglobulin formed by the malignant plasma cell. Response or lack of response to chemotherapy can be documented by measurement of daily excretion of BJP. Appearance of BJ proteinuria in patients with myeloma usually signifies a transition to a more aggressive form of disease. BJP themselves are probably malignant entities with pathophysiologic effects, the most important of which are those on the kidney. Renal dysfunction in patients with BJ proteinuria may appear as proximal or distal tubular effects, nephrotic syndrome, or the development of azotemia. BJP are indicators of the primary or myeloma-associated form of amyloidosis. A poorer prognosis is associated with patients with lambda type of BJP than those with kappa type. Chemotherapy is recom-

mended for symptomatic myeloma patients with BJP in their plasma or urine. Caution should be exercised for asymptomatic patients with BJP because of the toxicity and potential mutagenic of the drugs used. (15 Refs)

33. SEROLOGIC IDENTIFICATION OF EARLY MEMBERS OF THE T CELL LINEAGE.

Berman JW, Basch RS
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J Immunol; 128(4):1718-1722 1982

The SC-1 antigen, identified by thymus-absorbed rabbit antimouse brain antiserum, is present on multipotential stem cells. Its presence on cells of the T lineage has been examined by immunofluorescence, and we have demonstrated that it is also a marker for thymic development. Although it is present on the majority of fetal and neonatal thymocytes, its expression declines rapidly and, as early as 1 mo after birth, adult levels are reached. In normal animals, these do not change during adult life, even in mice destined to develop a T cell leukemia. SC-1 does reappear transiently on cells in the regenerating thymus of sublethally irradiated mice. Although the antigen is not associated with preleukemic changes in the thymus, it is expressed on some cells of all spontaneous T lymphomas, and it is uniformly present on tissue culture lines of cell lymphomas. (Author abstract) (11 Refs)

34. AN ACTIVATION-INHIBITION MODEL OF CYCLIC GRANULOPOIESIS IN CHRONIC GRANULOCYTIC LEUKEMIA.

MacDonald N
Dept. Natural Philosophy, Univ. Glasgow, Glasgow G12 8QQ, Scotland
Math Biosci; 54(1/2):61-70 1981

An activation-inhibition model of the cyclic granulopoiesis in CGL is presented. In chronic granulocytic leukemia (CGL), granulocyte counts may vary in cycles of 30-70 days, suggesting the operation of a negative feedback control mechanism with a time delay equal to the maturing time of the granulocytes. In the model, mature monocytes are assumed to secrete a stimulating agent and mature granulocytes an inhibiting agent. The inhibiting agent reduces the monocytic production of the stimulating agent. Leukemic granulocytes are assumed to produce less inhibiting agent than normal granulocytes. The long cycles of granulopoiesis in CGL may indicate that the leukemic granulocytes have an abnormally long maturation time. The model predicts that a declining production of inhibiting factor should be less marked when oscillations are present than for typical leukemic granulocytes; the cyclic oscillations of counts are predicted to be accompanied by monocyte oscillations. (21 Refs)

35. ESTABLISHMENT AND CHARACTERIZATION OF AN EPSTEIN-BARR VIRUS-NEGATIVE LYMPHOMA B-CELL LINE FROM A PATIENT WITH A DIFFUSE LARGE CELL LYMPHOMA.

Dillman RO, Handley HH, Royston I
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Cancer Res; 42(4):1368-1373 1982

Cell line (LNPL) was established from a tumor biopsy of a nasopharyngeal 'histiocytic' lymphoma composed of large noncleaved B-cells. LNPL expressed immunoglobulin M kappa surface immunoglobulin, as did the original tumor. LNPL also expressed Ia antigen but lacked Epstein-Barr virus nuclear antigen. It exhibited a translocation between chromosomes 8 and 14 which has been described in certain other malignant lymphoproliferative disorders. An autologous T-cell line lacked the translocation between chromosomes 8 and 14. LNPL is being used as an immunogen to produce monoclonal antibodies in our laboratory. Such cell lines may facilitate identification of lymphoma-associated surface antigens. (Author abstract) (36 Refs)

EXPERIMENTAL STUDIES INVOLVING CHEMICAL AGENTS AND IRRADIATION

36. EFFECT OF PHENOBARBITAL ON THE DEVELOPMENT OF TUMORS IN MICE TREATED NEONATALLY WITH N-ETHYL-N-NITROSOUREA.

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Dept. Cancer Res., Res. Inst. Nuclear Medicine and Biology, Hiroshima Univ., Kasumi 1-2-3,, Minami-ku, Hiroshima 734, Japan
Gan; 73(1):111-114 1982

This study was undertaken to evaluate the effect of phenobarbital on the development of neurogenic tumors induced in mice by neonatal administration of N-ethyl-N-nitrosourea (ENU). A total of 185 A/He mice was divided into four groups. Continuous oral administration of phenobarbital (0.05%) in drinking water was commenced 4 wk after birth in Group I. A single injection of 40 mg/kg of ENU was given subcutaneously on the back within 24 hr after birth in Group II. After neonatal injection of ENU, phenobarbital was commenced 4 wk after birth in Group III. Group IV was the untreated control. The experiment was terminated 12 mo after birth. The serum level of phenobarbital at the end of the experiment was 8.7 ug/ml in Group I and 7.0 ug/ml in Group III. Neurogenic tumors were induced only in groups treated with ENU. The incidence was 5.7% in Group II and 10.9% in Group III, though the difference between the two groups was not statistically significant. A total of three tumors (3.0%) was induced in the central nervous system and five tumors (5.1%) in the peripheral nervous system. Histologically, the former were oligodendroglioma and the latter were schwannoma. Lung tumors, lymphomas and hepatic tumors were also induced by ENU, and in male mice phenobarbital had a suppressing effect on the development of liver tumors. (Author abstract) (19 Refs)

37. EFFECT OF ETHANOL ON VINYL CHLORIDE CARCINOGENESIS.

Radike MJ, Stemmer KL, Bingham E
Dept. Environmental Health, Kettering Lab., Univ. Cincinnati Medical Center, 3223 Eden Ave., Cincinnati, OH, 45267
Environ Health Perspect; 41:59-62 1981

The potential cocarcinogenicity of ethanol with vinyl chloride (VC) was studied in male Sprague-Dawley rats. A total of 320 rats (80 rats in each of four groups) were studied: Group 1 was exposed to VC (600 ppm, 4 hr/day, 5 days/wk for 1 yr), Group 2 was exposed to VC and ethanol (5% in water, beginning 4 wk before the start of VC exposure and continuing for life), Group 3 was exposed only to ethanol, and Group 4 was exposed only to filtered air. At 18 mo rats exposed to VC showed an av weight loss of approx 9%. At 18 mo the survival rate was 40% for Group 1, 18% for Group 2, 73% for Group

3, and 70% for Group 4. Angiosarcomas were found in 23% of Group 1, 50% of Group 2, and 0% of Groups 3 and 4. Hepatocellular carcinomas were found in 44% of Group 1, 60% of Group 2, 10% of Group 3, and 0% of Group 4. Lymphosarcomas were found in all groups but most frequently in Group 2. Endocrine tumors were found in 57 rats in Group 3, compared with 29 in Group 1, 30 in Group 2, and 8 in Group 4. Some rats developed more than one angiosarcoma or carcinoma. Results indicate that ethanol has a strong cocarcinogenic effect in rats exposed to VC. (8 Refs)

38. OBSERVATIONS OF THE SITE-SPECIFIC CARCINOGENICITY OF VINYL CHLORIDE TO HUMANS.

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Office Carcinogen Identification and Classification, Health Standards, Program, Occupational Safety and Health Admin. U. S. Dept. Labor, Washington, DC, 20210
Environ Health Perspect; 41:89-94 1981

Studies of site-specific carcinogenicity of vinyl chloride (VC) are reviewed. Problems encountered included relative insensitivity to carcinogenic response at low risk sites due to small sample size, and characteristics of method and design that prevent adequate interpretation of results. Restriction of disease definition resulted in obscuring some sites that might otherwise have shown significant excess risk. Four of eight studies indicated a significant risk of liver cancer following exposure to VC, although the liver had been confirmed as a site of VC-carcinogenesis by other studies. Problems with studies of liver cancer included insufficient exposure and observation times. Some studies classify liver cancer with other cancers of the digestive tract. Overall data from at least one study of cancers of the digestive tract indicate a reduction in mortality among exposed workers. An excess of mortality due to CNS cancers was indicated by five of eight studies. Some studies classified CNS cancers with nonspecific 'other' categories. Data for lung cancer mortality suggest a significant increase in risk for workers exposed to VC. Data for cancers of the lymphatic and hematopoietic systems are suggestive but not conclusive. Overall data indicates that the carcinogenic effect of VC is not limited to the liver. (12 Refs)

39. MUTAGENIC AND TUMOURIGENIC PROPERTIES OF THE SPORES OF ASPERGILLUS CLAVATUS.

Blyth W, Hardy JC
Dept. Botany, Univ. Edinburgh, King's Building, Edinburgh EH9 3JH, England
Br J Cancer; 45(1):105-117 1982

Spore walls of a sputum-derived isolate of Aspergillus clavatus yielded mutagen(s) when their extracts were fractionally precipitated with ethanol following alkaline hydrolysis. After spores were given by nasal inoculation to 6-8-wk-old CF-1 mice, light and electron microscopy of lung sections showed that they had been readily phagocytosed by the polymorphonuclear leukocytes and alveolar macrophages mobilized during early allergic alveolitis in immunized mice. The formation of phagosomes was followed in thioglycollate-stimulated peritoneal macrophages grown in vitro. Unimmunized mice showed a comparable lung reaction, attributed to pulmonary mycotoxicosis, and revealed a rising incidence of lung tumors, from 25% at 2 months from inoculation, to 27.3% at 6 and to 55.5% at 8. Mean numbers of tumors per lung rose from 1.0 to 2.2. Total tumors, including lymphomas, reached a final incidence of 77.7% at 8 months, when control animals were tumor-free. Tumor development correlated with the retention of apparently intact spores within giant cells probably derived from aggregates of alveolar macrophages. The implications of these findings in the light of the known history of human exposure to such spores is discussed. (Author abstract) (34 Refs)

40. RAT LYMPHOID LEUKEMIA OF T CELL TYPE INDUCED BY 7,12-DIMETHYLBENZ(ALPHA)ANTHRACENE. IMMUNOLOGICAL AND ENZYMOLOGICAL CHARACTERIZATION.

Peter I, Gal F, Sugar J, Medgyesi G
Natl. Oncological Inst - Res. Inst. Oncopathology, Rath Gyorgy-u. 7-9, 1122, Budapest, Hungary
Oncology; 39(2):113-117 1982

Lymphoid leukemia induced by 7,12-dimethylbenz(a)anthracene (DMBA) in rats and maintained by serial intraperitoneal transplantations in newborn rats was subjected to immunological and enzymological characterization. The Thy-1 antigen positivity rendered evidence for the T cell origin of the leukemia studied. Expression of cell surface complement binding receptors and patterns of cytoplasmic acid phosphatase and non-specific acid alpha-naphthyl acetate esterase enzymes drew the attention to the dominance of lymphoblasts and prolymphocytes. (Author abstract) (33 Refs)

41. THE CHARACTERIZATION OF TRYPAN BLUE-INDUCED TUMORS IN WISTAR RATS.

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Am J Pathol; 106(3):326-331 1982

Trypan blue is an azo dye widely used for testing cell viability. The dye has been identified as a mutagen and a carcinogen. In some strains of rats, particularly Wistar rats, chronic exposure induces a reticuloendothelial neoplasm, predominantly in the liver. These tumors were studied with the use of immunologic cell membrane markers, electron microscopy, and histochemistry to characterize tumor cell type. The authors have studied this tumor in two inbred lines of Wistar rats to compare the efficacy of two previously described dye regimens on tumor incidence and to ascertain whether a short, intense exposure was as effective as chronic protracted exposure. No significant difference in tumor incidence was observed between the two regimens. These studies suggest that the tumor is composed of a macrophage-like cell that retains some characteristics of normal macrophages and that it is a reproducible model for carcinogen-induced lymphoreticular disease that may be of value in the study of some human lymphomas. (Author abstract) (22 Refs)

EXPERIMENTAL STUDIES: DNA TUMOR VIRUSES

42. IMMUNOGLOBULIN PROPERTIES OF EPSTEIN-BARR VIRUS TRANSFORMED HUMAN UMBILICAL CORD AND ADULT PERIPHERAL BLOOD LYMPHOCYTES.

Konowalchuk J, Speirs JI, Perelmutter L
Lab. Centre Disease Control, Health Protection Branch, Health and Welfare Canada, Ottawa K1A 0L2, Canada
Cell Immunol; 67(1):190-196 1982

Lymphocytes from umbilical cords and peripheral adult blood were transformed with Epstein-Barr virus. Cultures of these transformed cells were studied for cell-associated and secreted immunoglobulins (Ig) and for their stability after long-term culture. The adult cell lines produced intracellular and extracellular Ig of all five classes but there was a paucity of IgA in cord cell cultures. Cells producing cytoplasmic Ig were at least 10 times more numerous than those secreting Ig. Both cord and adult lines appeared relatively stable after months of culture indicating that both may be useful in the preparation of immunological reagents. (Author abstract) (21 Refs)

43. ALPHA2HS GLYCOPROTEIN BINDS TO LYMPHOCYTES TRANSFORMED BY EPSTEIN-BARR VIRUS.

Lewis JG, Crosier PS, Andre CM
Dept. Clinical Biochemistry, Christchurch Clinical Sch. Medicine, Christchurch Hosp., Christchurch, New Zealand
FEBS Lett; 138(1):37-39 1982

Binding of alpha2HS glycoprotein to Epstein-Barr virus (EBV)-transformed peripheral blood lymphocytes was studied by indirect immunofluorescence and by direct counts of cell-bound 125I-alpha2HS glycoprotein. This glycoprotein binds appreciably to EBV-transformed, but not to normal autologous, untransformed, lymphocytes (dissociation constant 5.0 x 10(-7) M, with 0.5 x 10(6) sites/cell). Binding of transformed cells is not blocked by deoxyribonuclease pretreatment, but can be partially blocked by ribonuclease or pronase pretreatment. (11 Refs)

44. ETIOPATHOGENESIS OF AVIAN MAREK'S LYMPHOMA DURING HERPES-RETROVIRUS INFECTION.

Iakovleva LS, Plakhov IV, Voronov AV, Mazurenko NP
All-Union Cancer Res. Inst., Moscow, USSR
Eksp Onkol; 4(1):18-21 1982

Interactions of Marek's disease virus (MDV) and Rous-associated virus (RAV-49) were studied in chickens. The incidence of Marek's lymphoma (ML) in chickens infected im with MDV (Group I) was 46.4%, compared with 48.4% in chickens subjected to im infection with RAV-49 and contact infection with MDV (Group II). The incidence of ML in chickens subjected to contact infection with MDV was only 14.7%. Indirect immunofluorescence showed predominance of T-cell markers in ML from Group I as well as from Group II. Analysis of MDV antigen in the epithelium of feather follicles showed the presence of virus-specific precipitating antigen starting from day 10 after im infection with MDV. In case of mixed infection, MDV antigen was first detected in 4-wk-old chickens. (18 Refs) (In RUS)

45. ALTERATIONS IN MICROFILAMENTOUS AND MICROTUBULAR STRUCTURES ACCOMPANIED BY CELL GROWTH OF SV40-TRANSFORMED CLONAL MACROPHAGES, LINE 28-12 AND ITS SUBLINE.

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Cell Struct Funct; 6(4):329-339 1981

Morphological patterns of sets of actively growing and stationary simian virus 40 (SV40)-transformed macrophages of the clonal line 28-12, obtained from SV40-infected cultures of mouse bone marrow cells, were compared with those of the slowly growing subline 28-12(Ara) isolated from cytosine arabinoside-treated cultures. Transmission and scanning electron microscopic observations revealed microfilamentous and microtubular structures in the cells. Bundles of 70 A microfilaments were found in fully-transformed, actively growing 28-12 cells but not in minimally-transformed, stationary 28-12 cells, an observation which inconsistent with other studies. A decrease in microtubules apparently occurs in actively growing cells which have high levels of SV40 T-antigen, although evidence is not unequivocal. Response of the cells to colchicine shows that cytoskeletal structures, including microtubules, are affected by transformation. The 28-12(Ara) cells, which are considered moderately transformed cells, have a significant amount of SV40 T antigen, fewer microtubules than either type of 28-12 cells, lower response to colchicine, and slower growth, but the cells also have a phagocytic capacity. (32 Refs)

EXPERIMENTAL STUDIES: RNA TUMOR VIRUSES

46. PRIMARY STRUCTURE ANALYSIS OF THE MAJOR INTERNAL PROTEIN P24 OF HUMAN TYPE C T-CELL LEUKEMIA VIRUS.

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Proc Natl Acad Sci USA; 79(4,part1):1291-1294 1982

A human type C retrovirus [human T-cell leukemia (lymphoma) virus; HTLV], recently isolated from young adult patients with cutaneous T-cell lymphoma or leukemia, was not detectably related to other known animal retroviruses in molecular hybridization studies, by comparison of reverse transcriptase and the major core protein p24. The p24 core protein was purified to homogeneity. The amino acid composition, the COOH-terminal amino acid, and the NH2-terminal amino acid sequence of the first 25 residues of this major internal structural protein were determined. These results were then compared to the known structure of the internal core protein of other retroviruses. The compositional data reveal that HTLV p24 is chemically distinct from p30-p24 of other animal retroviruses, in agreement with the earlier immunological analyses. However, HTLV p24 shares the common NH2-terminal proline and COOH-terminal leucine of all mammalian type C viral p30s. In addition, like bovine leukemia virus (BLV), HTLV lacks the common prolylleucylarginine tripeptide and the larger conserved region found near the NH2 terminus of the other mammalian type C viral p30s. Alignment of the amino acid sequence of HTLV p24 with previously determined sequences of

other retrovirus proteins, including BLV p24, reveals statistically significant sequence homology only to BLV. The results reported here demonstrate that HTLV p24 is related to but chemically distinct from the major core protein of other retroviruses. Similarly, previous results showed that there was no immunological crossreactivity of the p24 protein and reverse transcriptase of HTLV with other retroviruses, including BLV, and no nucleic acid sequence homology. However, the present results, combined with the common size o f the p24 and reverse transcriptase, suggest that HTLV may be closer to BLV than any other known retrovirus. (Author abstract) (23 Refs)

47. A CRUCIAL ROLE OF THE H-2 D LOCUS IN THE REGULATION OF BOTH THE D- AND THE K-ASSOCIATED CYTOTOXIC T LYMPHOCYTE RESPONSE AGAINST MOLONEY LEUKEMIA VIRUS, DEMONSTRATED WITH TWO DB MUTANTS.

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J Immunol; 128(3):1360-1364 1982

Previous studies have shown that the CTL response of C57BL/6(B6,H-2b) mice against Moloney leukemia virus is H-2 Db-restricted. In the current paper, we analyze the role of the H-2 Db locus in the CTL response against Moloney virus with two strains of mice carrying a mutation in the H-2 Db locus: B6.C-H-2bm13(bm13) and B6.C-H-2bm14(bm14). The influence of the D locus was seen at two levels. First, neither of the two Db-mutant targets could be recognized by Db-restricted CTL, as demonstrated with B10.A(4R) (Kk Db) and B6 (Kb Db) effector cells. Second, mutation at the Db locus strongly altered the character of the response, either by causing nonresponsiveness (bm 14 effector) or by increasing the Kb-associated component of the CTL response (bm13 effector). These findings indicate that a single genetic element, H-2 D in this instance, determines the restriction specificity and regulates the magnitude of the CTL response. Cold target inhibition studies showed that either the restriction specificities of Dbm13 and Kb in the CTL response to this virus are indistinguishable or that the Dbm12-associated component of bm13 CTL is negligible. Experiments with (B6 x bm13)F1 and (B6 x bm14)F1 hybrid responding cells demonstrated a decisive role of H-2 on the antigen-presenting cells used for restimulation in vitro: primed F1 responding cells mounted CTL responses with the H-2 preference and magnitude of the parental cell type used for restimulation in vitro. Our findings strongly support the notion that Type I MHC molecules regulate the magnitude and specificity of the CTL response against viruses. (Author abstract) (29 Refs)

48. CROSS-REACTIONS BETWEEN TUMOR CELLS AND ALLOGENEIC NORMAL TISSUES. INHIBITION OF A SYNGENEIC LYMPHOMA OUTGROWTH IN H-2 AND NON-H-2 ALLOIMMUNE BALB/C MICE.

Parmiani G, Sensi ML, Carbone G, Colombo M, Pierotti M, Ballinari D, Hilgers J, Hilkens J
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Int J Cancer; 29(3):323-332 1982

To test whether alloimmunization with H-2 or/and non-H-2 different normal tissues may increase the immunity to syngeneic tumors, groups of BALB/c (H-2d) mice were immunized with a series of allogeneic lymphoid cells and then challenged ip with syngeneic lymphoma cells. The outgrowth of otherwise lethal doses of the Moloney virus-induced lymphoma YC8 and of its clones was inhibited in BALB/c mice immune to DBA/2 (H-2d), C3Hf (H-2k), C3H.SW (H-2b), C3H.OH (H-2c2) and to B10 background tissue but not in mice immunized to A/He, BALB.K (H-2k) or BALB.B (H-2b) normal tissues. Anti-YC8 effect was also induced by immunizing BALB/c recipients with a pool of five different allogeneic cell lines which included C3Hf, C57BL/6J (H-2b), N:NIH (H-2q), B10.M (H-2f), and DBA/2 lymphoid cells. No growth inhibition of other BALB/c lymphomas induced by Moloney virus (LSTRA), x-rays (RL male I) or urethane (UR-I) was evident in alloimmune mice. In vivo transfer of growth inhibition of YC8 was obtained with BALB/c anti-B10.D2 peritoneal exudate cells in a Winn assay. The ability of these alloimmune lymphoid cells to delay significantly the survival time of BALB/c mice injected with the mixture of immune cell and YC8 cells was abrogated by anti-Thy 1.2 plus C' treatment. In addition, nu/nu BALB/c mice were unable to develop resistance to YC8 outgrowth after alloimmunization. The results of this study show that (1) syngeneic growth of a lymphoma can be prevented by autoimmunization with normal cells, (2) this cross-reaction involved non-H-2 antigens, (3) the phenomenon appeared to be mediated by T cells. (Author abstract) (35 Refs)

49. DEFINITION OF ALIEN H-2 DETERMINANTS ON A FRIEND LEUKEMIA BY ANALYSIS OF ALLOREACTIVITY OF CTL FROM PRIMARY MLC.

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J Immunogenet; 8(6):493-508 1981

An in vivo passaged subline (HFL/d) of Friend virus-induced leukemia of BALB/c origin expressed alien H-2 antigens as determined by reactivity with cytolytic T lymphocytes (CTL). This subline originated from an in vitro passaged subline HFL/d-tc, which when inoculated into BALB/c mice induced weak transplantation resistance. During adaptation to in vivo growth the new ascitic subline HFL/d apparently acquired the capacity to stimulate a cytotoxic response to H-2d antigens, but lost the ability to be lysed by CTL or antisera directed to its H-2d determinants. The presence of H-2d antigen of HFL/d recognizable by CTL was further confirmed by the inhibition of lysis of H-2d targets by HFL/d cold targets. HFL/d stimulated in primary mixed lymphocyte culture (MLC) the generation of CTL which could lyse HFL/d through recognition of non-H-2d determinants not detectable on the parent in vivo passaged subline HFL/d-tc. The alloantigens on HFL/d were typed by generating CTL in primary MLC with HFL/d as stimulator, and measuring reactivity to targets with known H-2 antigens, and was confirmed by assessing recognition of HFL/d targets by CTL generated in primary MLC with stimulators expressing known H-2 antigens. HFL/d expresses K d and Dd determinants derived from its strain of origin, alien determinants similar to Kb and Db antigens, and at least one additional determinant not present on normal H-2d or H-2b cells. CTL generated in MLC in a sensitive tool for examination of tumors for the presence of alien and/or cross-reactive H-2 determinants. (39 Refs)

50. THE IN VITRO GENERATION OF H-2-RESTRICTED CYTOTOXIC T CELLS TO AKR/GROSS LEUKEMIA VIRUS-INDUCED TUMORS. I. REQUIREMENT FOR STIMULATION WITH ALLOGENEIC LEUKEMIA CELLS IN VIVO.

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J Immunol; 128(3):1043-1049 1982

We have reported previously that vigorously lytic preparations of H-2-restricted C57BL/6 (H-2b) murine T cells specific for the subset of endogenous AKR leukemia virus-induced tumors that express the Gross cell surface antigen, including EmaleG2, can be raised. The generation of such CTL was accomplished by in vivo priming with an allogeneic AKR leukemic line followed by in vitro coculture of spleen cells from primed mice with irradiated GCSA+ tumors of H-2b haplotype. The results of the present report strongly suggest that the form of primary in vivo stimulation is crucial to the generation of such CTL. Examination of the four GCSA+ tumor cells of H-2b haplotype that are susceptible target cells in this system confirmed the requirement for in vivo alloantigenic stimulation. Thus, the two syngeneic tumor targets, EmaleG2 and EL4(S), were inefficient, whereas two H-2 congenic tumor targets, AKR H-2bSL1 and B.GV (BALB.B-derived), were efficient when used as priming cells. It appeared that the generation of H-2-restricted C57BL/6 CTL to AKR/Gross leukemia virus-induced tumors required concomitant in vivo stimulation with both target antigen and alloantigens. Although these alloantigens were not required to be H-2 encoded, it appeared they had to be present on the same cell that expressed the target antigens to exert their stimulatory effect. (33 Refs)

51. A NEW MURINE LYMPHOCYTE ALLOANTIGEN, LY-21.2, MAPPING TO THE SEVENTH CHROMOSOME.

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Immunogenetics; 15(3):239-250 1982

Using a monoclonal antibody raised by fusing spleen cells from A/J mice, immunized with B10.A splenocytes and lymph-node cells, with a BALB/c myeloma, we have described a new surface alloantigen, Ly-21.2. Ly-21.2 is present in varying amounts in all lymphoid tissues, is not detectable in the brain, kidney, lung or erythrocytes, and is found in only trace amounts in the liver. Strain distribution studies showed that Ly-21.2 is present in all strains examined, including B10, except the A strain and segregation analysis of (A/J x B10)F2 mice showed that Ly-21.2 expression (1) is encoded by one gene and (2) is linked to albinism on chromosome 7. Studies performed on mice developing T-cell leukemia showed that, regardless of the etiologic agent, Ly-21.2 expression increases dramatically in mice with overt leukemia. In addition, preliminary studies suggest that expression of Ly-21.2 is linked to increased susceptibility of mice to Friend-virus-induced erythroleukemia. (Author abstract) (27 Refs)

52. INTRACELLULAR LOCALIZATION OF CERTAIN MEMBRANE GLYCOPROTEINS IN MOUSE T-LYMPHOMA CELLS USING IMMUNOFERRITIN STAINING OF ULTRATHIN FROZEN SECTIONS.

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J Cell Physiol; 110(2):203-212 1982

Morphology observed with frozen thin sections of mouse T-lymphoma cells was compared with that of epon thin sections, with special emphasis on membranous organelles. The intracellular localization of several types of membrane glycoproteins in the T-lymphoma cell system was examined. No significant differences were found between epon and frozen thin sections. Immunoferritin staining on frozen thin sections was specific, reliable, and suitable for intracellular localization of various membrane glycoproteins based on studies using antibodies directed against Thy-1, a T-cell-specific membrane glycoprotein. Many of the membranous cellular structures of the T-lymphoma cells contained the concanavalin A-specific sugars, alpha-D-mannose and alpha-D-glucose. The intracellular distribution of the viral membrane protein, gp 69/71, was studied in lymphoma cells known to be productively infected with a C-type RNA virus. Gp 69/71 molecules were detected on the surface of free and budding C-type viral particles. Occasionally, gp 69/71 was also found in discontinuous patchlike arrays along certain regions of the T-lymphoma cell surface. Viral antigens were found in terminal regions of certain flattened rough endoplasmic reticulum membranes, in a diffuse pattern at certain regions of the stacked Golgi membranes, and in clustered arrays within small vesicle-like structures either close to the plasma membrane or at an apparent point of contact between an individual vesicle and the plasma membrane. (19 Refs)

53. FACTORS DETERMINING THE SUSCEPTIBILITY OF NIH SWISS MICE TO ERYTHROLEUKEMIA INDUCED BY FRIEND MURINE LEUKEMIA VIRUS.

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Virology; 117(2):357-365 1982

Helper-independent virus from a molecularly cloned stock of Friend murine leukemia virus (F-MuLV) induces an erythroproliferative disease characterized by splenomegaly and severe anemia in newborn mice of certain susceptible strains, such as NIH Swiss. With age, NIH Swiss mice become resistant to this F-MuLV-induced erythroleukemia. Resistance is not correlated with the replication of the input Friend MuLV but is correlated with the replication of Friend MCF viruses in the spleens of infected mice. Treatment of adult NIH Swiss mice with x-irradiation, phenylhydrazine, or silica before injection of F-MuLV increases the replication of MCF viruses in the spleens of these mice and renders them significantly more susceptible to erythroleukemia. In contrast to mice infected with F-MuLV as newborns or as x-irradiated adults, untreated 6-wk-old NIH Swiss mice develop a good humoral immune response to MCF gp70. These results suggest that the resistance of adult NIH Swiss mice to erythroleukemia induced by F-MuLV is due to the lack of replication of Friend MCF viruses in these mice because of (1) a good immune response to the virus, (2) the lack of a suitable number of susceptible target cells, or (3) both. (Author abstract) (27 Refs)

54. LYMPHATIC LEUKEMIA AND RETRIEVAL OF DEFECTIVE FRIEND VIRUS IN ATHYMIC NUDE RATS.

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Life Sciences Div., SRI International, Menlo Park, CA, 94025
Proc Soc Exp Biol Med; 169(3):316-319 1982

Inoculation of Friend virus (FV) into newborn athymic rats, followed by infection with lymphatic leukemia virus (LLV) resulted in development of leukemia in two rats, while the other two were aleukemic when the experiment was terminated after 135 days. Following injection of LLV into newborn athymic mice, viremia was detected in 20 days with subsequent death in approx 100 days. All seven young adult BALB/c mice infected with the same preparation of FV developed histologically confirmed Friend disease. Athymic newborn rats inoculated with LLV were later xenografted with cells from virus-free, FV-induced tumor grown in vitro. Cell free extracts of the tumors that developed induced typical Friend disease in newborn mice. Because the rat apparently lacks target cells for FV replication, the entire output of virus must have originated in the tumor itself, which is in marked contrast to findings of earlier experiments in BALB/c mice. (10 Refs)

55. MOBILITY OF ENDOGENOUS ECOTROPIC MURINE LEUKEMIA VIRAL GENOMES WITHIN MOUSE CHROMOSOMAL DNA AND INTEGRATION OF A MINK CELL FOCUS-FORMING VIRUS-TYPE RECOMBINANT PROVIRUS IN THE GERM LINE.

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J Virol; 41(3):901-908 1982

Characterization of endogenous ecotropic Akv proviruses in DNA of low and high leukemic mouse strains revealed the presence of one to six copies of the Akv genome per haploid genome equivalent integrated in the germ line. Low leukemic strains analyzed so far contained only one complete copy of the Akv proviral DNA. The site of integration varied among strains, although genetically related strains often carried the Akv proviral gene in the same chromosomal site. The different substrains of the AKR mouse dis played the presence of variable numbers (2 to 6) of Akv genomes. In all substrains one Akv genome was present in an identical chromosomal site; this locus probably comprised the progenitor genome. Closely related substrains had several Akv proviral DNAs integrated in common sites. The accumulation of Akv genomes in the germ line of the AKR/FuRdA strain is likely the result of independent integration events, since backcross studies with the Akv-negative 129 strain showed random segregation of all six proviral loci. The AKR/Cnb strain carried a recombinant provirus in the germ line. This provirus resembled in structure the AKR mink cell focus-forming viruses, which are generated by somatic recombination during leukemogenesis. Therefore, the germline amplication of Akv proviral DNAs occurs most likely through infection of embryonic cells by circulating virus. (Author abstract) (28 Refs)

56. ISOLATION OF TWO VARIANTS OF DUAL ECOTROPIC AND XENOTROPIC RETROVIRUS FROM THYMUSES OF MICE INOCULATED AS NEWBORNS WITH GROSS MURINE LEUKAEMIA VIRUS.

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Ann Virol; 132(2):207-216 1981

Two variants of dual ecotropic and xenotropic retrovirus isolated from thymuses of C3HeB/Fe mice inoculated ip as newborns with a leukemogenic dose of Gross murine leukemia virus passage A are described. Thymus cells of individual mice were cocultivated with mink murine leukemia viruses (MvlLu). Virus detections were preformed weekly by reverse transcriptase assays with each culture supernatant from the cocultures and by parallel XC tests. By this procedure, the XC negative and mink cell infectious virus Th2P1 was isolated. This virus replicated efficiently in mink MvlLu cells and in mouse SC1 cells. When subconfluent MvlLu cultures were infected with Th2P1, 6-10 days later numerous foci of morphological change characterized by thickened cell sheets surrounded by rounded cells with vacuoles were observed. In C3HeB/Fe mice inoculated ip as newborns with 0.3 ml of the Th2P1 virus suspension, no leukemia developed during 500 days after virus inoculation. Th4P1 was isolated from a mouse free from leukemic symptoms. Host range studies revealed that this virus replicated efficiently in MvlLu, SIRC, NRK, and SCI cells, but not in human breast cancer cells. For mouse cells, Th4P1 showed N tropism, and did not induce any morphological change neither in heterogenous nor in mouse cells. Th4P1 was XC negative, possessed helper activites towards both S+L- mink and S+L- mouse cells, and was neutralized significantly by anti-xenotropic and anti-ecotropic virus serum. (19 Refs)

57. VIRUS CLONED FROM THE RAUSCHER VIRUS COMPLEX INDUCES ERYTHROBLASTOSIS AND THYMIC LYMPHOMA.

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Virology; 118(1):225-228 1982

The pathogenicity of two ecotropic viruses cloned from a Rauscher virus complex (RV), that had been passaged in the mouse, has been studied. One of the viruses, R-MuLV, gives rise to syncytia in the XC test (XC-positive), the other, R-XC-virus, does not (XC-negative). Both cloned viruses induce erythroblastosis and thymic lymphoma after inoculation into newborn NIH Swiss mice. Another clonal isolate of R-MuLV, from a stock which has been propagated in tissue culture, similarly induces both diseases when injected into newborn NIH Swiss mice. All R-MuLV and R-XC- induced splenic and thymic tumors produced, in addition to the injected virus, mink cell focus-inducing virus. This is consistent with the idea that MCF viruses are the actual (proximal) viruses causing the proliferative processes in the hematopoietic cells which lead to the different diseases. The finding that an R-MCF virus, which in most cases induces erythroblastosis, can also induce thymic lymphoma at a low frequency suggests that both diseases could be induced by the same MCF virus. (Author abstract) (18 Refs)

58. MIXED INFECTION OF BALB/C MICE WITH RAUSCHER LEUKEMIA VIRUS AND L FORMS OF LISTERIA.

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Eksp Onkol; 4(1):21-25 1982

Characteristic features of mixed infection with Rauscher's leukemia virus (RLV) and L forms of listeria (LL) were studied in BALB/c mice. The 2-mo-old mice were inoculated ip with the mixture of RLV and LL (Group I), with RLV alone (Group II), or with LL alone (Group III). By day 60 after inoculation, 87% of mice in Group I died of leukemia, compared with 36% in Group II. All mice in Group III were free of leukemia. Majority of mice in Group I died on days 30-40 after inoculation, while majority of mice in Group II died on days 40-50 after the inoculation. All mice infected with RLV and LL showed marked pathological changes in the spleen: severe erythroblastosis with massive necrotic and hemorrhagic foci were observed on days 42-49 after mixed infection. Mice infected with RLV alone showed hyperplasia of the lymphoid tissue of the spleen and foci of the erythroid hematopoiesis. Mice infected with LL alone had only slight changes in the spleen. It was suggested that stimulation of RLV is associated with immunosuppressive effect of LL. (9 Refs) (In RUS)

59. BIOPHYSICAL AND BIOLOGICAL CHARACTERISTICS OF A MURINE LEUKEMIA RETROVIRUS.

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Medicina (B Aires); 41(Suppl):207-214 1981

Constitution of murine leukemia retrovirus was investigated. Female BALB mice 1.5-2 mo old weighing 18-20 g were inoculated with PLLV-T2 virus which induced leukemia. Acellular extracts were prepared from leukemic spleens. Filtration, ultracentrifugation, bioassay, and in vivo titration were performed and sedimentation rate were calculated. Based on the obtained data it was concluded that PLLV-T2 virus is a Type C retrovirus. (16 Refs) (In SPA)

60. CHARACTERIZATION OF A HIGHLY ONCOGENIC MURINE LEUKEMIA VIRUS FROM WILD MICE.

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Int J Cancer; 29(3):345-350 1982

We have isolated a highly lymphomagenic wild mouse virus by passage of a weakly oncogenic amphotropic murine leukemia virus (MuLV-A) in NIH Swiss mice. This virus is similar in host range, interference and neutralization properties to that of the inoculated amphotropic virus but is distinct from it biochemically and causes lymphomas in 90-100% of mice within 1-2 mo. Our results indicate that this highly oncogenic virus is a recombinant of wild mouse MuLV-A and sequences related to env gene region of the endogenous xenotropic virus of NIH Swiss mice. (Author abstract) (45 Refs)

61. COMPLETE AMINO ACID SEQUENCE OF THE GROUP-SPECIFIC ANTIGEN GENE-ENCODED PHOSPHORYLATED PROTEINS OF MOUSE LEUKEMIA VIRUSES.

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J Biol Chem; 257(6):3007-3013 1982

The complete amino acid sequence of the group-specific antigen gene-encoded RNA binding phosphoprotein p12 has been determined for both Rauscher and Moloney leukemia viruses. Large fragments generated by acid, cyanogen bromide and hydroxylamine cleavage, and Staphylococcus aureus V8 protease digestion were subjected to automated sequencing. Both Rauscher and Moloney p12 are composed of 84 amino acids arranged in alternating variable and conserved regions. The homology between the conserved internal and COOH-terminal regions is greater than 95%, but the NH2-terminal and internal variable regions show 59 and 51% homology, respectively. The role of such regions in the type-specific biological activities of these molecules is discussed. (Author abstract) (42 Refs)

62. MOLECULAR CLONING OF MURINE ENDOGENOUS VIRAL SEQUENCES AND EXPRESSION OF A NEWLY CONSTRUCTED RECOMBINANT MURINE LEUKEMIA VIRUS DNA IN TRANSFECTED MINK CELLS.

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Proc Natl Acad Sci USA; 79(5):1398-1402 1982

In the process of molecularly cloning unintegrated proviral DNA from NIH-3T3 mouse cells infected with Rauscher murine leukemia virus, we observed the occurrence of clones with inserts smaller than the expected Rauscher murine leukemia virus fragments. The insert of one of these clones, lambda.Xe-1, was characterized in more detail. It had a size of 3.5 kilobases. The restriction map was similar but not identical to that of the envelope regions of Moloney and Rauscher murine leukemia viruses. After ligation to previously cloned Moloney murine leukemia viral sequences and transfection of the ligated DNA into mink lung cells a nondefective xenotropic murine leukemia virus, XH-19, was isolated. Restriction mapping of provital DNA isolated from mink lung cells chronically infected with XH-19 showed the presence of Moloney murine leukemia virus-derived sequences coupled to xenotropic viral sequences. (Author abstract) (24 Refs)

63. SELECTIVE EFFECT OF FELINE LEUKAEMIA VIRUS ON EARLY ERYTHROID PRECURSORS.

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Nature; 296(5853):156-158 1982

In a survey of feline leukemia virus (FeLV) subgroups in naturally infected cats, FeLV-C was not observed in 98 clinically normal cats but was found in 9/32 anemic cats. Subgroup C viruses from three of these anemic cats were biologically cloned and used to infect neonatal kittens. Each isolate produced a pure red cell hypoplasia (RCH), the pathology of which resembled that previously described for FeLV-C/Sarma. To determine the effect of subgroup C viruses on hematopoietic precursor cells, 3.5 x 10(5) focus-inducing units of

FeLV-C/Sarma were inoculated ip within 24 hr of birth into specific pathogen-free, randomly bred cats. Control and infected cats were bled weekly to determine their blood constituents and virus status. FeLV-C/Sarma infected cats showed a rapid depletion of early erythroid precursors (burst-forming units-erythroid; BFU-E) while the proportion of the myeloid precursor (granulocyte-macrophage colony-forming cells; GM-CFC) in the bone marrow remained normal. While the mechanism of FeLV-C-induced depletion of BFU-E is unknown, any hypothesis to explain the above findings must account for the remarkable selective effect of FeLV-C in producing RCH with normal levels of GM-CFC and circulating leukocytes. (25 Refs)

64. ULTRASTRUCTURAL EXPRESSION OF INCOMPLETE VIRUS-LIKE PARTICLES IN MURINE MYELOBLASTS GROWING IN VITRO.

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Ann Virol; 132(2):295-302 1981

The expression and development of incomplete virus-like particles (VLP) within cytoplasmic inclusion bodies of murine myeloblastic leukemia cells growing in vitro, morphologically differen t from A-, B-, and C-type particles are discussed. Cell lines DB18 and DB16 were studied. The cell lines have been characterized biologically for the presence of granulocyte-macrophage-specific intracellular enzymes, and both synthesize myeloperoxidase and lysozyme. Electron microscope examination revealed that the cytoplasm of all the cell sections examined from both lines contained inclusion bodies (IB). The number of IB/section ranged from 3 to over 50. Electron-dense subunits appear to form circular particles with or without tail formation. Extracellular budding of C-type virus particles from the cell membrane could not be seen in any over 200 cells examined from each of the two lines. Complete C-type particles could be found in two extracellular areas of those cells examined. They were present in a restricted area together with smaller particles which are probably incomplete viruses. The very large number of cytoplasmic inclusion bodies, many of which contain VLP in different stages of their development, suggest that those IB are probably viroplasms, rather than cytoplasmic organelles. (13 Refs)

65. COMPARATIVE LEUKEMIA: OF MICE AND MEN.

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Departamento de Leucemia Experimental, Instituto de Investigaciones, Hematologicas Academia Nacional de Medicina, Buenos Aires, Argentina
Medicina (B Aires); 41(Suppl):199-206 1981

Results obtained using three experimental models testing for viral activity in human lymphoma over a 24-yr period are reviewed. Human lymphoma cells inoculated into mice indicated cross-immunity between lymphoma associated antigens. Sarcoma 180 intrasplenic inoculation into mice increased tumor growth and metastases, an effect never observed with subcutaneous transplants; splenectomy increased tumor rejection. Human cells were obtained from biopsy of lymph node (LN), bone marrow (BM), or from in vitro lines of Burkitt, Epstein-Barr 1, Kudi, Jijoye, P3J, and the lymphosarcoma lines GH7 and LDLT. Controls were from normal human muscle (5 specimens), tonsils (6), and normal BM (4). After 10 days animals were killed, spleens homogenized and injected ip into 1-mo-old BALB/c mice, and the inoculated animals observed for 2 yr. Of the LN biopsy specimens from 93 patients with lymphoma, only 9 produced short term (10-43 days) leukemia; such results were reproducible 2 or 3 times in two cases and were not obtained in controls. Long latency leukemias (18 mo) were produced in 49% of animals. Experiments with AKR lymphoma cells gave similar results. Human lymphoblastoid cells injected into cylinders implanted in mice produced tumorigenesis in 62%, compared to 31% of animals implanted with normal lymphocytes and 45% with empty cylinders. The AKR cells in cylinders produced a 66% incidence of fibrosarcomas. When AKR cells or thymocytes were used as targets, antibodies were detected in sera from 66% of 118 acute lymphoid leukemia cases, 75% of 44 Hodgkin's lymphoma cases, and 0% of 171 normal blood donors; AKR lymphoma in mice produced similar results. The findings indicate that human lymphoma cells may behave like AKR lymphoma cells bearing antigenic determinants of Gross virus, which induces murine leukemia. (28 Refs)

66. SUPPRESSION OF SPONTANEOUS LYMPHOMA BY PREVIOUSLY UNDISCOVERED DOMINANT GENES IN CROSSES OF HIGH- AND LOW-INCIDENCE MOUSE STRAINS.

Chen S, Lilly F
(c/o Lilly) Dept. Genetics, Albert Einstein Coll. Medicine, Bronx, NY, 10461
Virology; 118(1):76-85 1982

Crosses of mice of the high-lymphoma mouse strains, AKR and C58, with mice of the low-lymphoma strains, C57L, DBA/1, and DBA/2, produce F1 generations with low and late incidences of the spontaneous disease. Backcross populations, obtained from high-lymphoma parental strain x low-lymphoma F1 matings, showed lymphoma incidences of approx 75%, indicating that the low lymphoma incidence in F1 mice of these crosses was due to the simultaneous presence of at least two independently segregating dominant genes inherited from the low-lymphoma parental strain. In none of the three crosses was lymphoma resistance linked to the Fv-1 locus, and in only one (AKR x C57L) was H-2 type a significant determinant of the disease. This finding indicates that previously undiscovered genes possess the capacity to suppress spontaneous murine lymphoma. Studies of the expression of endogenous ecotropic and xenotropic murine leukemia viruses in mice of these crosses suggest that one of the new genes involved in lymphoma suppression may act by delaying the expression of xenotropic virus. (Author abstract) (25 Refs)

67. AT LEAST TWO REGIONS OF THE VIRAL GENOME DETERMINE THE ONCOGENIC POTENTIAL OF AVIAN LEUKOSIS VIRUSES.

Robinson HL, Blais BM, Tsichlis PN, Coffin JM
Worcester Foundation Experimental Biology, Shrewsbury, MA, 01545
Proc Natl Acad Sci USA; 79(4,part1):1225-1229 1982

Recombinants of oncogenic and nononcogenic avian leukosis viruses were tested for their oncogenic potential in chickens. The results indicate that at least two regions of the viral genome determine the oncogenic potential of these viruses. The first region contains sequences that control viral mRNA synthesis. These sequences determine the potential of a virus to induce a low incidence of lymphomas, carcinomas, chondrosarcomas, fibrosarcomas, and osteopetrosis. The second region lies outside the sequences that control viral mRNA synthesis. These sequences determine the ability of a virus to induce a high incidence of lymphomas or osteopetrosis. (Author abstract) (41 Refs)

68. NUCLEAR LOCALIZATION AND DNA BINDING OF THE TRANSFORMING GENE PRODUCT OF AVIAN MYELOCYTOMATOSIS VIRUS.

Donner P, Greiser-Wilke I, Moelling K
Max-Planck-Institut fur Molekulare Genetik, Berlin-Dahlem, Ihnestrasse 63-73, 1 Berlin 33, W. Germany
Nature; 296(5854):262-266 1982

A previous study has shown that the activated cellular gene in certain lymphomas was homologous to the oncogene of an acute avian leukemia virus, MC29. In MC29, the oncogene is fused to the viral structural gene, gag. The mol wt of the fused gene is 110,000 (110 K) and is designated as p110gag-myc. For further analysis, the 110 K protein was purified from the 35S-methionine-labeled MC29-transformed quail embryo fibroblast cell line MC29-Q8-NP (which does not produce virus particles, but expresses the transforming protein gag-myc) by an immune affinity column containing protein A-Sepharose to which monoclonal anti-p19 IgG was covalently coupled in conditions which link the constant region of the IgG molecule to the solid phase. Immunofluorescence studies and cell fractionation of MC29-transformed fibroblasts indicate that the 110 K protein is predominantly located in the nucleus. The purified protein was found to bind to double-stranded DNA. These properties may be related to the role of the protein in transformation. (22 Refs)

69. ISOLATION AND BIOCHEMICAL CHARACTERIZATION OF PARTIALLY TRANSFORMATION-DEFECTIVE MUTANTS OF AVIAN MYELOCYTOMATOSIS VIRUS STRAIN MC29: LOCALIZATION OF THE MUTATION TO THE MYC DOMAIN OF THE 110,000-DALTON GAG-MYC POLYPROTEIN.

Ramsay GM, Hayman MJ
Imperial Cancer Res. Fund, London WC2A 3PX, England
J Virol; 41(3):745-753 1982

Recently, we isolated three mutants of MC29 virus which, although able to transform fibroblasts with the same efficiency as wild-type MC29, were 100-fold less efficient at transforming macrophages. In this study we found that MC29-transformed quail producer cell line Q10 was able to generate these partially transformation-defective mutants at a high frequency. Using tryptic peptide mapping, we determined that the smaller gag-myc polyproteins encoded by the transformation-defective viruses had lost myc-specific tryptic peptides. This suggested that the mutations which resulted in the transformation-defective viruses being inefficient at transforming macrophages were located in the v-myc sequence and thus directly implicated v-myc and the gag-myc polyprotein in transformation by MC29. (Author abstract) (35 Refs)

70. DELETIONS WITHIN THE TRANSFORMATION-SPECIFIC RNA SEQUENCES OF ACUTE LEUKEMIA VIRUS MC29 GIVE RISE TO PARTIALLY TRANSFORMATION-DEFECTIVE MUTANTS.

Bister K, Ramsay GM, Hayman MJ
Max-Planck-Institut fur Molekulare Genetik, D-1000 Berlin 33, W. Germany
J Virol; 41(3):754-766 1982

The viral RNAs of three nonconditional mutants of avian myelocytomatosis virus MC29 were analyzed. These mutants, which were originally isolated from the quail producer line Q10 and were designated 10A, 10C, and 10H, have lost most of the ability to transform hematopoietic cells in vitro and to induce tumors in vivo, but they still transform cultured fibroblasts with the same efficiency as wild-type (wt) MC29. Electrophoretic analyses showed that the mutant genomic RNAs were smaller than the 5.7-kilobase genome of wt MC29; the genomes of mutants 10A, 10C, and 10H were about 5.5, 5.3, and 5.1 kilobases long, respectively. Analyses of the transformation-specific sequences of these mutant RNAs by a combination of T1 oligonucleotide fingerprinting and hybridization with cDNA from the transformation-specific sequences myc of wt MC29 or competition hybridization including wt MC29 RNA revealed that deletions of myc-specific sequences had occurred. The deletions in all three mutants overlapped, since they all had lost one particular myc-specific oligonucleotide. In agreement with the size of the genomic RNAs, mutants 10C and 10H had lost two additional myc oligonucleotides, and mutant 10A contained a modified myc oligonucleotide. The locations of the deletions were deduced from comparisons with previously established oligonucleotide maps of several members of the MC29 subgroup of acute leukemia viruses and by hybridization of wt and mutant RNAs to molecularly cloned subgenomic fragments of wt MC29 proviral DNA, representing the 5' and 3' domains of the myc sequence. We found that the deleted sequences represented overlapping internal segments of the myc sequence and that the borders of myc with the partial complements of the virion genes gag and env appeared to be conserved in mutant and wt MC29 RNAs. The correlation between the altered transforming potential for hematopoietic cells and the partial deletion of myc in the mutant RNAs provided direct genetic evidence for the involvement of myc in oncogenesis. However, the unaffected efficiency of these mutants in fibroblast transformation suggested that the deleted sequences are not essential for the fibroblast-transforming potential of the onc gene of MC29. (Author abstract) (31 Refs)

71. AN IGM-PRODUCING B LYMPHOBLASTOID CELL LINE ESTABLISHED FROM LYMPHOMAS INDUCED BY A NON-DEFECTIVE RETICULOENDOTHELIOSIS VIRUS.

Nazerian K, Witter RL, Crittenden LB, Noori-Daloii MR, Kung HJ
Regional Poultry Res. Lab., U.S. Dept. Agriculture, 3606, East Mount Hope Road, East Lansing, MI, 48823
J Gen Virol; 58(part2):351-360 1982

Chick syncytial virus (CSV), a strain of avian reticuloendotheliosis virus (REV) causes lymphoid tumors in chickens after a prolonged incubation period. A number of CSV-induced tumors were examined for cell surface antigen and were found to be of the B cell type and to produce immunoglobulin. Attempts were made to grow in vitro cell lines from CSV-induced tumors and a lymphoblastoid cell line was established from a liver tumor of a chicken that was inoculated with CSV via the yolk sac in embryo. The donor chicken was viremic at the time the tumor was removed. The cell line is designated RECC-RP13, it produces non-defective REV, is a B cell type and it produces IgM. It is free from infection with endogenous and exogenous avian leukosis virus (ALV) and has an increased number of chromosomes. Sequences specific to REV were detected in at least four sites in cellular DNA from RECC-RP13. Sequences specific to ALV DNA, beyond that normally found in 15I5 x 71 cells, were not found in DNA from this cell line. (Author abstract) (31 Refs)

REVIEWS AND OTHER RELATED STUDIES

72. ONCOGENES.

Bishop JM
Univ. California, San Francisco, CA
Sci Am; 246(3):80-84,87-92,154 1982

Recent developments in cancer research concerning inducement of cancerous growth are reviewed. Some tumor viruses (TV) are oncogenic only in animals that are not hosts in nature, others are oncogenic only in their natural host. Transformation of cultured cells by TV makes possible the examination of the interaction of a TV with a host cell under controlled conditions, thus avoiding the difficulties associated with experiments in animals. Some viruses have a single gene which can induce tumors, or in some cases, a few such 'oncogenes'. Retroviruses (RV) are the only TV with an RNA genome. The src oncogene of Rous sarcoma virus is discussed. The protein encoded by src is a 60,000 mol wt phosphoprotein. Phosphorylation of tyrosine is a common characteristic of oncogene-encoded enzymes and also has a role in regulating the growth of normal cells. The mutational hypothesis proposes that viral oncogenes differ from their cellular progenitors as a result of mutations introduced when the cellular genes were copied into the RV genome. The dosage hypothesis suggests that RV oncogenes overburden cells with too much essentially normal proteins carrying out normal functions. Excessive activity might tip the balance of regulation toward incessant growth. In tumors induced by the chicken lymphoma viruses, the viral DNA is almost always inserted into cellular DNA in the immediate vicinity of a single cellular oncogene, and the expression of the cellular oncogene is greatly amplified. Gene-length bits of DNA isolated from some tumors can transmit the property of cancerous growth when they are introduced into previously normal cells in culture. (4 Refs)

73. CURRENT STATUS OF CYTOGENETIC STUDIES IN ANIMAL TUMORS WITH SPECIAL REFERENCE TO NONRANDOM CHROMOSOME CHANGES.

Sasaki M
Chromosome Res. Unit, Hokkaido Univ., Faculty Science, Sapporo 060, Japan
Cancer Genet Cytogenet; 5(2):153-172 1982

The current status of animal tumor cytogenetics is reviewed with particular attention given to nonrandom karyotypic rearrangements and their implications in animal neoplasia. Tumors of the mouse discussed include thymic lymphoma, plasmacytoma, myeloid leukemia, hematologic, and nonhematologic tumors. Tumors of the rat discussed include leukemias, sarcomas, and transplanted tumors or cell lines studied by banding. Chromosome control of tumors in cultured hamster cells (Syrian and Chinese) is reviewed. (158 Refs)

74. ASSOCIATION OF THE EPSTEIN-BARR VIRUS WITH NASOPHARYNGEAL CARCINOMA.

Henle W, Henle G
Joseph Stokes, Jr., Res. Inst., Childrens Hosp. Philadelphia, Philadelphia, PA, 19104
Cancer Research in the People's Republic of China and the United States of America: Epidemiology, Causation and New Approaches to Therapy, Proceedings of a Conference held in New York, 28-29, March, 1980. Marks PA, ed. New York, Grune and Stratton, 273 pp., 1981.

Association found using an immunofluorescence test (IFT) for detection of Epstein-Barr virus (EBV) in Burkitt's lymphoma and for titration of antibodies to the virus is discussed. Antibodies measured in the original IFT were directed against viral capsid antigen, which is present in every virus-producing cell. Approaches used for linking a virus with a human malignancy have been detection of viral fingerprints in the tumor, malignant transformation of normal cells by the virus in vitro, induction of tumors in non-human primates or other animals by injection of the virus, and demonstration of a broad spectrum and higher titers of antibodies to virus-related antigens in patients compared to controls and their relation to prognosis of the patients. EBV-specific serology may serve to monitor the effectiveness of therapy and to warn of imminent relapses or metastases before they become clinically evident. (20 Refs)

75. CAUSES OF LEUKEMIAS AND CANCER: RECENT PROGRESS.

Bernard J
bd. de Perolles 53, 1700 Fribourg, Switzerland
Rev Med Suisse Romande; 102(1):95-103 1982

Roles of viruses, radiation, and toxic chemical substances in the development of cancer are discussed. Burkitt's lymphoma (BL), a B-cell lymphoma predominantly localized in facial bones and found most frequently in certain areas of Africa, was one of the first cancers to be related to a virus, Epstein Barr virus (EBV). EBV virus and its antibodies are found in BL patients. EBV virus, the infective agent in mononucleosis, has been shown to cause BL in marmosets. BL shows high correlations with geographic areas with levels of malaria, with chromosome translocation 8:14, and with lower socioeconomic groups. Viruses have also been implicated in cervix cancer (herpes virus), liver cancer (hepatitis B), and Hodgkin's disease. Evidence of radiation-induced cancers has been gained from studies of physicians, radiologists, and scientists exposed to radiation and of Hiroshima survivors. The relationship between radiation and cancer development is significant but varies among individuals. Dietary factors, such as tobacco (lung, bladder, and digestive cancers), alcohol (cirrhosis and liver cancer), and diet in general (high lipid diet and breast cancer) have been related to increased incidences of cancer. Leukemia has been observed in Hodgkin's disease patients treated with chemotherapy. A high incidence of lymphomas has been noted in patients who have undergone organ transplants. The role of heredity and geography in the etiology of cancer is discussed. (no Refs) (In FRE)

76. A COMPARISON OF THE PATHOBIOLOGY AND EPIDEMIOLOGY OF CANCERS ASSOCIATED WITH VIRUSES IN HUMANS AND ANIMALS.

Essex M, Gutensohn N
Dept. Microbiology, Harvard Univ. Sch. Public Health, 665 Huntington Ave., Boston, MA, 02115
Prog Med Virol; 27:114-126 1981

Several oncogenic viruses in animals (chicken, cat, ox, gibbon, rabbit) are discussed in terms of characteristics and epidemiological features and are compared with human malignancies most likely to be caused by a virus (leukemias, Hodgkin's disease, Burkitt's lymphoma, cervical cancer, nasopharyngeal cancer, and primary hepatocellular carcinoma). Cancers of industrialized countries tend to be associated with environmental or dietary agents, whereas those in the developing world are likely to be of viral origin, suggesting that a vaccination program would have a profound effect in developing countries. (52 Refs)

77. FELINE LEUKAEMIA VIRUS INFECTION.

Randles JL
P.O. Box 1, 4920 Kei Road, South Africa
J S Afr Vet Assoc; 52(3):259-265 1981

Feline leukemia virus (FeLV) is reviewed with emphasis on clinical aspects. Etiology, incidence, transmission, source of infection, immunity, susceptible hosts, pathogenesis, and pathology are presented. Clinical findings, diagnosis, and treatment, of malignant neoplasms and non-neoplastic diseases involving FeLV are discussed. Possible methods of control are described. (24 Refs)

78. THE HANDBOOK OF CANCER IMMUNOLOGY, VOLUME 7. IMMUNE FUNCTION AND DYSFUNCTION IN RELATION TO CANCER.

Waters H
NIH, Bethesda, MD
The Handbook of Cancer Immunology, Volume 7. Immune Function and Dysfunction in Relation to Cancer. New York, Garland STPM Press, 372 pp., 1981.

Aspects of immune function and dysfunction as they relate to cancer are presented. Immunological surveillance is discussed with consideration of the thymus, macrophages, cytotoxic cells, and immunodepression in cancer patients. Immune responses to challenge, including cellular and humoral factors, and the role of these factors in immune suppression are considered. Other topics include regulation of immune response, immunobiology of chemotaxis and metastases, and the role of macrophages and other cells in carcinogenesis. Macrophage arginase and arginine consumption are related to tumor growth. Also d iscussed are rejection and enhancement of grafts, the role of antigens and antibodies in idiotype regulation and T-lymphocyte modulation, immunoregulation via modified amino groups, immunity and tolerance to transplantation antigens, and production of specific unresponsiveness to tissue allografts by immunosuppression and donor antigen. Normal and abnormal conditions, as well as intermediate conditions are compared. Discussion of topics includes review, original findings, and speculation about future investigative efforts. (1420 Refs)

79. LEUKEMIA OVERVIEW.

Burchenal JH
Clinical Investigation, Memorial Sloan-Kettering Cancer Center, New York, NY
Cancer- Achievements, Challenges, and Prospects for the 1980s, Proceedings of an International Conference held in New York, 14-16 September, 1980. Vol. 2, Memorial Sloan-Kettering Cancer Center New York, NY. Burchenal, J. H. and Oettgen, H. F., eds. (New York, Grune and Stratton), 944 pp., 1981.

Progress in diagnosis, understanding, and treatment of leukemia is reviewed. Etiology, history of the development of chemotherapeutic agents, development of curative combination therapy, use of biochemical and genetic markers in therapy, and in vitro cell line studies are discussed. Increased understanding of the leukemic process at both the basic and clinical levels, the large number of drugs already available, and increasing development of new agents will make possible control of most leukemias. (55 Refs)

80. THE CHRONIC LEUKEMIAS.

Canellos GP
Div. Medical Oncology, Sidney Farber Cancer Inst., Boston, MA
Cancer- Achievements, Challenges, and Prospects for the 1980s, Proceedings of an International Conference held in New York, 14-16 September, 1980. Vol. 2, Memorial Sloan-Kettering Cancer Center New York, NY. Burchenal, J. H. and Oettgen, H. F., eds. (New York, Grune and Stratton), 944 pp., 1981.

The biology of chronic granulocytic leukemia is discussed in relation to the Philadelphia chromosome abnormality, chemotherapy, and allogeneic transplantation in the chronic phase. An antiserum specific for the Philadelphia chromosome bearing cell lines would be valuable in cell sorting and in the use of immunologic techniques to eradicate leukemic cells. Chronic lymphocytic leukemia (CLL) is discussed with respect to biology, chemotherapy, and radiotherapy; CLL remains extremely difficult to eradicate by intensive therapy. (11 Refs)

81. CELL SURFACE GLYCOPROTEIN MARKERS FOR NEOPLASIA.

Bhavanandan VP, Davidson EA
Dept. Biological Chemistry, Milton S. Hershey Medical Center, Hershey, PA, 17033
Methods Cancer Res; 19:53-105 1982

Glycoproteins that serve as cell surface markers of neoplasia are described biochemically, in relation to viral transformation, and for various animal and human cells, and the methods em ployed are reviewed. The animal tumors and derived cell lines discussed include the following: neuroblastoma, melanoma, ascites, hepatoma, mammary carcinoma, lung carcinoma, and leukemias and lymphomas. Glycoprotein cell surface markers in human cells are reviewed in relation to melanoma, mammary carcinoma, lung carcinoma, colon carcinoma, ovarian carcinoma, and neuroblastoma. Metabolic labeling, isolation, purification, mapping, and structural analysis techniques applied to glycoproteins are reviewed. Future studies in this field will probably take advantage of improved methods such as isoelectric focusing gels, lectin affinity chromatography, and monoclonal antibodies. Ultimately the metabolic and genetic origin of each macromolecule must be determined. In the meantime, glycoprotein cell surface marker studies may be expected to contribute to diagnostic and immunologic approaches to management of disease. (313 Refs)

82. NATURE OF CANCER.

Dulbecco R
Salk Inst., La Jolla, CA
Boll Soc Ital Biol Sper; 57(18):21-30 1981

Fight against cancer is discussed. Two approaches are considered: a pragmatic one, using any means even those that are only partially effective, and a more general type trying to elucidate cellular changes, and their mechanisms and causes. The following topics are included oncogenic viruses and genes, differences in oncogenic mechanisms of sarcoma and leukemia viruses, promotor, chemical oncogenic induction, initiation, facilitation, differences between species (man, rat, mouse), and validity of animal testing. (no Refs) (In ITA)

83. REVERSION OF CANCER CELLS.

Boiron M

Service des Maladies du Sang, Hopital Saint-Louis, Institut de Recherches d'Hematologie et d'Oncologie, 2, place du Docteur A. Fournier, 75475 Paris Cedex 10, France

Pathol Biol (Paris); 30(3):133-135 1982

Three models of cancer cell reversion are presented, and the following reversion of cells transformed in vitro by oncogenic viruses, collection of normal cells after blockage of differentiation in leukemic cells, and possible differentiation in teratocarcinomas leading to loss of malignancy. In vitro, certain DNA and RNA viruses can transform normal cells into malignant cells with modifications of growth parameters, cellular surface characteristics, cytoskeleton, and nucleotide pool; these virus-transformed cells are capable of tumorigenesis in vivo. Temperature-sensitive mutants of the viral oncogene include normal cells produced from virus-transformed cells. In another model, apparently normal revertant cells may be observed at low frequencies; in vivo, the cells rarely loose their oncogenic potential completely. Dimethylsulfoxide modifies the morphology of Friend's leukemia cells thereby r'easing the inhibition that prevents the normal execution of the genetic program; normal differentiation coincides with lost of malignancy . Other leukemia models of reversion are described. Reversion of teratocarcinoma cells is discussed in relation to treatment with retinoids. (no Refs) (In FRE)

84. CURRENT CANCER RESEARCH ON PEDIATRIC NEOPLASMS (SPECIAL LISTING).

International Cancer Research Data Bank Program Office
NCI, Westwood Building, Room 10A18, Bethesda, MD, 20205

Pediatric Neoplasms (Special Listing) This Title is Available Through National Technical Information Service, Springfield, VA, as NTISUB/PB81-929411; 52pp. 1981

Special Listings of Current Cancer Research Projects are a service of the International Cancer Research Data Bank (ICRDB) program of the National Cancer Institute. Each listing contains descriptions of ongoing projects in one selected cancer research area. The descriptions are provided by cancer scientists in about 50 different countries. Etiological and epidemiological studies of pediatric neoplasms are discussed with respect to familial, genetic and congenital factors and the incidence of childhood cancer; in utero exposure to exogenous estrogens and other agents and the incidence of childhood cancer; iatrogenic exposure to radiation and drugs and the incidence of childhood cancer; demographic and other etiologic factors and the incidence of pediatric leukemia, lymphoma, nephroblastoma, and other solid tumors; and other environmental and etiologic factors. Preclinical chemotherapy studies in model systems of pediatric neoplasms are desribed. Clinical diagnosis and prognostic factors in childhood cancer are discussed. Therapy of leukemia, lymphoma, histiocytosis, intracranial tumors, neuroblastoma, nephroblastoma, retinoblastoma, rhabdomyosarcoma, and other solid tumors is outlined and pharmacokinetics, therapeutic complications, and patient supportive care are discussed. Clinical studies by cooperative groups, broad clinical programs, and educational programs are reviewed.

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NOTICE OF CURRENT REVIEWS: CARCINOGENESIS

As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

CHEMICAL CARCINOGENESIS

1. IARC MONOGRAPHS ON THE EVALUATION OF THE CARCINOGENIC RISK OF CHEMICALS TO MAN. SOME ANTINEOPLASTIC AND IMMUNOSUPPRESSIVE AGENTS.
Schmahl D
International Agency for Cancer Research, Lyon, France
IARC Mongr Eval Carcinog Risk Chem Hum 26: 411 pp., 1981.

2. BIOCHEMICAL TOXICOLOGY OF BENZENE.
Snyder R, Longacre SL, Witmer CM, Kocsis JJ, Andrews LS, Lee EW
Dept. Pharmacology, Thomas Jefferson Univ., Philadelphia, PA, 19107
Rev Biochem Toxicol; 3:123-153 1981

3. A REVIEW OF THE MUTAGENICITY OF CHROMIUM.
Hatherill JR
Toxicology, Sch. Public Health, Univ. Michigan, Ann Arbor, MI, 48109
Drug Chem Toxicol; 4(3):185-195 1981

4. HORMONES AND BREAST CANCER.
Pike MC, Siiteri PK, Welsch CW
Dept. Family and Preventive Medicine, Univ. Southern California Sch. Medicine, Los Angeles, CA, 90033
Banbury Rep 8: 491 pp., 1981.

5. ORAL CONTRACEPTIVES: VOLUME 5.
Briggs MH, Briggs M
Deakin Univ., Geelong 3217, Australia
Oral Contraceptives: Volume 5. St. Albans, VT, Eden Medical Research Inc., Annual Research Reviews--Endocrinology, 331 pp., 1981.

6. EPIDEMIOLOGICAL STUDIES OF THE ROLE OF EXOGENOUS ESTROGENS IN THE ETIOLOGY OF BREAST CANCER.
Kelsey JL, Bulbrook RD, Koresman SG, Siiteri PK, Henderson BE
Dept. Epidemiology and Public Health, Yale Univ. Sch. Medicine, New Haven, CT, 06510
Banbury Rep; 8:215-228 1981

7. EFFECTS OF LONG-TERM EXPOSURE TO LOW LEVELS OF OZONE: A REVIEW.
Melton CE
Civil Aeromedical Inst., Federal Aviation Admin., Oklahoma City, OK, 73125
Aviat Space Environ Med; 53(2):105-111 1982

8. METABOLIC INTERACTIONS OF HYDROCARBONS WITH MAMMALIAN LUNG.
Smith BR, Bend JR
Lab. Pharmacology, Natl. Inst. Environmental Health Sciences, NIH, Research Triangle Park, NC, 27709
Rev Biochem Toxicol; 3:77-122 1981

9. REVIEW OF EXPERIMENTAL CARCINOGENESIS BY COMPOUNDS RELATED TO VINYL CHLORIDE.
Chu KC, Milman HA
NCI, Bethesda, MD, 20205
Environ Health Perspect; 41:211-220 1981

10. REVIEWS IN BIOCHEMICAL TOXICOLOGY.
Hodgson E, Bend JR, Philpot RM
North Carolina State Univ., Raleigh, NC
Rev Biochem Toxicol 3: 368 pp., 1981.

DIETARY FACTORS IN CARCINOGENESIS

11. ALCOHOL AND CANCER.
MacSween RN
Univ. Dept. Pathology, Western Infirmary, Glasgow, Scotland
Br Med Bull; 38(1):31-33 1982

12. THE TOXICOLOGY OF COCOA AND METHYLXANTHINES: A REVIEW OF THE LITERATURE.
Tarka SM
Life Sciences, Hershey Foods Corp., Corporate Technical Center, Hershey, PA
CRC Crit Rev Toxicol; 9(4):275-312 1982

13. IMPLICATIONS OF DIETARY FIBER BREAKDOWN IN THE HUMAN COLON.
Cummings JH, Stephen AM, Branch WJ
MRC Dunn Clinical Nutrition Centre, Old Addenbrookes Hosp., Cambridge, CB2 IQE, England
Banbury Rep; 7:71-81 1981

14. BILE SALTS AND OTHER CONSTITUENTS OF THE COLON AS TUMOR PROMOTERS.
Reddy BS, Tannenbaum SR, Montesano R, Correa P, Haenszel W, Wattenberg LW
Div. Nutrition, American Health Foundation, Naylor Dana Inst. for Disease Prevention, Valhalla, NY, 10595
Banbury Rep; 7:345-363 1981

15. MOLD PRODUCING CARCINOGENIC TOXINS IN FOOD PRODUCTS.
Preda N
Institutul de medicina si farmacie, Cluj-Napoca, Romania
Rev Chir [Oncol]; 20(1):1-9 1981
In RUM

16. THE MEANING OF CANCER 'DIETS'.
Jungi WF
Abt. f. Onkologie-Hamatologie, Medizinische Klinik C, CH-9007 St. Gallen, Switzerland
MMW; 124(2):26-28 1982
In GER

EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

17. RISK FACTORS FOR CERVICAL CANCER.
Hulka BS
Dept. Epidemiology, Rosenau Hall 201H, Univ. North Carolina, Chapel Hill, North Carolina, NC, 27514
J Chronic Dis; 35(1):3-11 1982

18. EPIDEMIOLOGY OF THE MOST FREQUENTLY OCCURRING TUMORS OF THE DIGESTIVE SYSTEM.
Naujoks-Heinrich S, Dolle W
Abteilung Innere Medizin I, Universitatsklinik, Otfried-Muller-Strasse 10, D-7400 Tubingen, W. Germany
Internist (Berlin); 23(1):1-9 1982
In GER

19. BLADDER CANCER.
Skrabanek P, Walsh A
Endocrine Oncology Unit, Mater Misericordiae Hosp., Dublin, Ireland
UICC Tech Rep Ser 60: 192 pp., 1981.

20. RECENT ADVANCES IN CANCER CYTOGENETICS.
Pogosiants EE
All-Union Cancer Res. Center, Moscow, USSR
Genetika; 17(12):2087-2099 1981
In RUS

21. CURRENT STATUS OF CYTOGENETIC STUDIES IN ANIMAL TUMORS WITH SPECIAL REFERENCE TO NONRANDOM CHROMOSOME CHANGES.
Sasaki M
Chromosome Res. Unit, Hokkaido Univ., Faculty Science, Sapporo 060, Japan
Cancer Genet Cytogenet; 5(2):153-172 1982

ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN CARCINOGENESIS

22. ASBESTOS-RELATED DISEASES.
Casey KR, Rom WN, Moatamed F
Building 512, RMCOEH, Univ. Utah Medical Center, Salt Lake City, UT, 84112
Clin Chest Med; 2(2):179-202 1981

23. NONASBESTOS FIBROUS MINERALS.
Lockey JE
Building 512, RMCOEH, Univ. Utah Medical Center, Salt Lake City, UT, 84112
Clin Chest Med; 2(2):203-218 1981

24. REVIEW OF EPIDEMIOLOGIC STUDY RESULTS OF VINYL CHLORIDE-RELATED COMPOUNDS.
Apfeldorf P, Infante PF
Office Carcinogen Identification and Classification, Health Standards, Programs, Occupational Safety and Health Admin. U. S. Dept. Labor, Washington, DC, 20210
Environ Health Perspect; 41:221-226 1981

25. CONCEPTS IN CAUSALITY: CHEMICALLY INDUCED HUMAN URINARY BLADDER CANCER.
Lower GM
Center Human Systems, Inst. Environmental Studies, Univ. Wisconsin, WARF Building, 610 Walnut St., Madison, WI, 53706
Cancer; 49(5):1056-1066 1982

CELLULAR AND MOLECULAR MECHANISMS IN CARCINOGENESIS

26. MOLECULAR MECHANISM OF ADAPTATION OF CELLS TO LOW LEVELS OF CARCINOGENIC AGENTS.
Villani G
Laboratoire de Pharmacologie et de Toxicologie Fondamentales, CNRS, 205, route de Narbonne, 31078 Toulouse Cedex, France
Pathol Biol (Paris); 30(2):117-123 1982
In FRE

27. MIGHT CANCER BE A FAILED RESPONSE TO RENEGADE MITOCHONDRIA?
Hartung J
Dept. Anesthesiology, State Univ. New York, Downstate Medical Center, Brooklyn, NY, 11203
J Theor Biol; 94(1):173-178 1982

MODIFICATION OF CARCINOGENESIS

28. EFFECT OF GEROPROTECTORS ON CARCINOGENESIS.
Anisimov VN
N. N. Petrov Res. Inst. Oncology, Leningrad, USSR
Usp Sovrem Biol; 92(3):455-472 1981
In RUS

29. RELATION OF NEUROLEPTIC DRUGS TO DEVELOPMENT AND GROWTH OF MAMMARY TUMORS.
Meites J, Aylworth CF
Dept. Physiology, Neuroendocrine Res. Lab., Michigan State Univ., East Lansing, MI, 48824
Banbury Rep; 8:365-376 1981

30. THE ACTIONS OF INSULIN AS A HORMONAL FACTOR IN BREAST CANCER.
Hilf R, Siiteri PK, Shellabarger, Koreman SG, Rosen, Nandi
Dept. Biochemistry and Univ. Rochester Cancer Center, Univ. Rochester, Rochester, NY, 14642
Banbury Rep; 8:317-337 1981

VIRAL AND IMMUNOLOGICAL ASPECTS OF CARCINOGENESIS

31. ONCOGENES.
Bishop JM
Univ. California, San Francisco, CA
Sci Am; 246(3):80-84,87-92,154 1982

32. HUMAN CANCERS AND HUMAN VIRUSES.
Waterson AP
Royal Postgraduate Medical Sch., London W12 0HS, England
Br Med J; 284(6314):446-448 1982

33. THE IMMUNOLOGY OF CANCER OF THE HEAD AND NECK WITH PARTICULAR REFERENCE TO ORAL CANCER.
Scully C
Univ. Dept. Oral Medicine and Pathology, Immunology Unit, Glasgow Dental Hosp., 378 Sauchiehall St., Glasgow G2 3JZ, Scotland
Oral Surg; 53(2):157-169 1982

METHODOLOGY IN CARCINOGENESIS RESEARCH

34. THE USE OF MAMMALIAN CELL MUTANTS TO STUDY THE MECHANISMS OF CARCINOGENESIS.
Trosko JE, Chang CC, Warren ST, Liu PK, Wade MH, Tsushimoto G
Dept. Pediatrics and Human Development, Michigan State Univ., Coll. Human Medicine, East Lansing, MI, 48824
Gann Monogr Cancer Res; 27:159-179 1982

35. BIOLOGICAL MONITORING IN THE IDENTIFICATION OF THE CANCER RISK OF INDIVIDUALS EXPOSED TO CHEMICAL CARCINOGENS.
Vainio H, Sorsa M, Rantanen J, Hemminki K, Aitio A
Inst. Occupational Health, Haartmaninkatu 1, SF-00290 Helsinki 29, Finland
Scand J Work Environ Health; 7(4):241-251 1981

36. A CRITICAL REVIEW OF BIOLOGICAL METHODS FOR THE DETECTION OF FUNGAL TOXINS IN FOODS AND FOODSTUFFS.
Watson DH, Lindsay DG
Food Science Div., Ministry of Agriculture, Fisheries, and Food, Great Westminster House, Horseferry Road, London SW1P 2AE, England
J Sci Food Agric; 33(1):59-67 1982

37. PITUITARY AND STEROID HORMONES IN RADIATION-INDUCED MAMMARY TUMORS.
Shellabarger CJ
Medical Dept., Brookhaven National Lab., Upton, NY, 11973
Banbury Rep; 8:339-351 1981

38. ASPERGILLUS NIDULANS: SYSTEMS AND RESULTS OF TESTS FOR CHEMICAL INDUCTION OF MITOTIC SEGREGATION AND MUTATION. I. DIPLOID AND DUPLICATION ASSAY SYSTEMS. A REPORT OF THE U. S. EPA GENE-TOX PROGRAM.
Kafer E, Scott BR, Dorn GL, Stafford R
Dept. Biology, McGill Univ., 1205 Ave. Docteur Penfield, Montreal H3A 1B1, Canada
Mutat Res; 98(1):1-48 1982

OTHER REVIEWS IN CARCINOGENESIS

39. MATHEMATICAL MODELS OF THE CELL CYCLE WITH A VIEW TO TUMOR STUDIES.
Bertuzzi A, Gandolfi A, Giovenco MA
Centro di Studio dei Sistemi di Controllo e Calcolo Automatici del C.N.R., Via Eudossiana 18, 00184 Rome, Italy
Math Biosci; 53(3/4):159-188 1981

40. NEOPLASMS IN DOMESTIC ANIMALS: A REVIEW OF EXPERIMENTAL AND SPONTANEOUS CARCINOGENESIS.
Madewell BR

Section Clinical Oncology, Dept. Veterinary Surgery, Univ. California, Davis, CA, 95616

Yale J Biol Med; 54(2):111-125 1981

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

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HE 20.3173/2:

EPIDEMIOLOGY AND ETIOLOGY OF HUMAN LYMPHORETICULAR MALIGNANCIES: VIRAL STUDIES

1. ISOLATION AND CHARACTERIZATION OF RETROVIRUS FROM CELL LINES OF HUMAN ADULT T-CELL LEUKEMIA AND ITS IMPLICATION IN THE DISEASE.

Yoshida M, Miyoshi I, Hinuma Y
Dept. Viral Oncology, Cancer Inst., Kami-Ikebukuro, Toshima-ku, Tokyo 170, Japan
Proc Natl Acad Sci USA; 79(6,part1):2031-2035 1982

A retrovirus (ATLV) was unequivocally demonstrated in human adult T-cell leukemia (ATL) cell lines by density (1.152-1.155 g/cm3) in a sucrose gradient, reverse transcriptase activity insensitive to actinomycin D, RNA labeled with [3H]uridine, and specific proteins with mol wt of 11,000, 14,000, 17,000, 24,000, and 45,000. Furthermore, cDNA prepared by endogenous reaction with detergent-treated virions hybridized to 35S RNA containing poly(A), which was inducible by IdUrd treatment of a T-cell line derived from leukemic cells of the ATL, and the integrated form of ATLV proviral DNA was detected in T-cell lines derived from ATL. The ATLV proviral DNA was also detected in fresh peripheral lymphocytes from all five patients with ATL tested so far but not in those from healthy adults. On the other hand, ATLV protein of Mr 42,000 was found to be at least one of the ATL-associated antigen(s) that were previously detected in ATL leukemic cells by all sera from patients with ATL. These findings on the close association of ATLV protein and proviral DNA with ATL are direct evidence for the possible involvement of the retrovirus ATLV in leukemogenesis of human ATL. (Author abstract) (18 Refs)

2. EXPRESSION OF CELLULAR HOMOLOGUES OF RETROVIRAL ONC GENES IN HUMAN HEMATOPOIETIC CELLS.

Westin EH, Wong-Staal F, Gelmann EP, Favera RD, Papas TS, Lautenberger JA, Eva A, Reddy EP, Tronick SR, Aaronson SA, Gallo RC
Lab. Tumor Cell Biology, NCI, NIH, Bethesda, MD, 20205
Proc Natl Acad Sci USA; 79(8,part1):2490-2494 1982

Total cellular poly(A)-enriched RNA from a variety of fresh human leukemic blood cells and hematopoietic cell lines was analyzed for homology with molecularly cloned DNA probes containing the ONC sequence of Abelson murine leukemia virus (Ab-MuLV), Harvey murine sarcoma virus (Ha-MuSV), simian sarcoma virus (SSV), and avian myelocytomatosis virus strain MC29. Results with the fresh blood cells paralleled those obtained with the cell lines. With Ab-MuLV and Ha-MuSV, multiple RNA bands were visualized in all cell types examined without significant variation in the relative intensities of the bands. When SSV was used as the probe, expression of related onc sequences was absent in all of the hematopoietic cell types examined except for one neoplastic T-cell line (HUT 102), which produces the human T-cell leukemia (lymphoma) retrovirus HTLV. In this cell line, a single band (4.2 kilobases) was observed. With MC29 as the probe, a single band of 2.7 kilobases was visualized in all cell types examined with only a one- to two-fold variation in intensity of hybridization. An exception was the promyelocytic cell line, HL60, which expressed approximately 10-fold more MC29-related onc sequences. With induction of differentiation of HL60 with either dimethyl sulfoxide or retinoic acid, a marked diminution in the amount of the MC29-related, but not the Ab-MuLV-related, onc message was observed. (Author abstract) (62 Refs)

3. DIFFERENTIAL EXPRESSION OF THE AMV GENE IN HUMAN HEMATOPOIETIC CELLS.

Westin EH, Gallo RC, Arya SK, Eva A, Souza LM, Baluda MA, Aaronson SA, Wong-Staal F
Lab. Tumor Cell Biology, Div. Cancer T[illegible]atment, NCI, Bethesda, MD, 20205
Proc Natl Acad Sci USA; 79(7):2194-2198 1982

Total cellular RNAs from a variety of fresh and culture-derived human hematopoietic neoplastic cell types at various stages of differentiation and human sarcoma, carcinoma, melanoma, and glioblastoma cell lines were enriched for poly(A)-containing sequences, fractionated by gel electrophoresis, and blot hybridized to a cloned DNA probe containing the transforming sequences (v-amv) of avian myeloblastosis virus (AMV), a virus known to cause myeloid leukemias in chickens. Expression of RNA sequences homologous to AMV was detected in all immature myeloid and lymphoid T cells in addition to single erythroid cell line examined, but not in mature T cells or in B cells, including lymphoblast cell lines derived from patients with Burkitt lymphoma. In addition, induction of the cell line HL60, a promyelocytic leukemia line, to differentiate with dimethyl sulfoxide or retinoic acid resulted in a reduction of the level of expression of the human cellular gene c-amv homologous to v-amv. There was no detectable c-amv mRNA in any of the solid tumor cell lines examined. Thus, expression of the human c-amv gene could be correlated with the stage of differentiation of different hematopoietic cell types determines by morphologic and marker studies. Expression of c-amv could not be correlated with the extent of methylation in HL60 and in HL60 induced to differentiate with dimethyl sulfoxide. (Author abstract) (48 Refs)

4. FINAL CASE REPORTING FROM THE UGANDAN PROSPECTIVE STUDY OF THE RELATIONSHIP BETWEEN EBV AND BURKITT'S LYMPHOMA.

Geser A, DeThe G, Lenoir G, Day NE, Williams EH
International Agency Res. Cancer, 150 Cours Albert Thomas, 69372 Lyon, France
Int J Cancer; 29(4):397-400 1982

A prospective epidemiological study was carried out in the West Nile District of Uganda from 1972 to 1979 in order to investigate the etiological role of the Epstein-Barr virus (EBV) in Burkitt's lymphoma (BL). By 1976, 14 BL cases had been detected among the 42,000 children originally bled in the study area. Testing of sera from BL candidates and neighborhood controls showed that children who develop BL later have EBV/VCA titers several dilutions higher than their age- and sex-matched neighbors. This appearance of a strong EBV activity long before BL development was taken as evidence of a causal role of EBV in BL. In order to add to the unique material of pre-bled BL cases, BL detection was continued up to March 1979 when field work became impossible in Uganda. Two additional pre-bled BL cases were found during this extension of the study. The serological and virological evaluation of these additional cases showed that the EBV/VCA titers, but not the EA and EBNA titers, were about two dilutions higher in the BL candidates than in the controls. Hybridization assays showed that both lymphomas contained EBV/DNA in the tumor cells. These additional results thus confirm the findings in the first 14 cases and strengthen the epidemiological evidence for a causal role of the EBV in endemic BL. (Author abstract) (10 Refs)

EPIDEMIOLOGY AND ETIOLOGY OF HUMAN LYMPHORETICULAR MALIGNANCIES: OTHER STUDIES

5. TRENDS IN CHILDHOOD LEUKAEMIA IN BRITAIN 1968-1978.

Stiller CA, Draper GJ
Childhood Cancer Res. Group, Univ. Oxford, Oxford OX2 6HE, England
Br J Cancer; 45(4):543-551 1982

Analysis of recent cancer registrations from Great Britain suggests that there has been an increase in the incidence of childhood acute lymphoid leukemia for children born after about 1964. The increase is statistically significant for boys aged 0-4 yr, and a lesser increase may also have occurred for girls in this age group. Reasons are given for believing that the increase is not purely an artifact attributable to improved registration procedures. Registration data from the Manchester Children's Tumor Registry, Denmark and Sweden support the suggestion that an increase has occurred. It is not at present possible to say whether a change in incidence will also be seen at higher ages or will be confined to the youngest children, who may represent an etiologically distinct sub-group. There is no obvious explanation for the findings reported here. (Author abstract) (16 Refs)

6. RISK FACTORS IN THE ETIOLOGY OF LEUKEMIA.

Popovic K, Pejin D, Stefanovic N, Belic A, Djokic M, Uzurov V, Mihajlovic M, Popovic S, Spasojevic J
Klinika za interne bolesti, Medicinski fakultet, Novi Sad, Yugoslavia
Med Pregl; 34(9/10):417-424 1981

Exogenous and endogenous risk factors in the etiology of leukemia were discussed. Of 125 patients with leukemia, 47 had the disease when the study was performed (21 acute leukemia and 26 chronic leukemia) and 78 were retrospective analyzed. Of the 21 patients (11 men, 10 women; 25-77 yr old) with acute leukemia, 4 of them were exposed to benzene, 1 to synthetic fertilizers, 1 to irradiation, and 5 had familial history of cancer. Patients Rh phenotype CeDee were 52.3% (37.54% found in the general population), and 61.9% were HLA phenotype A2 (48.6% found in general population). Of the 26 patients (9 men, 17 women; 20-90 yr old) with chronic leukemia, 1 of them received for prolonged amount of time phenylbutazone, 2 had familial history of cancer, and 2 belonged to families with leukemia. Of the 78 retrospective patients (33 men, 45 women; 10-90 yr old) with acute leukemia, 1 of them was exposed to benzene, 1 to pesticide, 1 to irradiation, 5 had familial history of cancer, and 8 suffered viral infections shortly before. Differentiation of blood groups in all the patients was similar to the general population. (30 Refs) (In SCR)

7. STATISTICAL LIMITATIONS IN RELATION TO SAMPLE SIZE.

Land CE
Environmental Epidemiology Branch, NCI, Bethesda, MD, 20205
Environ Health Perspect; 42:15-21 1981

Examples from radiation carcinogenesis are used to illustrate difficulties in estimating cancer risks for low doses of a carcinogen. Using direct estimation based on data from a population exposed to low doses, an example is given for a linear dose-response relationship for female breast cancer induced by exposure to sparsely ionizing radiation. Leukemia incidence data from a life span study of Nagasaki A-bomb survivors is used to illustrate curve fitting, by which higher dose data determine lower risk estimates. Although more is known about dose-response relationships for ionizing radiation than for any other environmental carcinogen, estimates of cancer risk for low radiation doses have sometimes disagreed by factors of 100 or more. (11 Refs)

8. RISK OF LEUKEMIA IN PATIENTS TREATED FOR HODGKIN'S DISEASE.

Brusamolino E, Lazzarino M, Salvaneschi L, Canevari A, Morra E, Castelli G, Pagnucco G, Isernia P, Bernasconi C
(c/o Bernasconi) Divisione di Ematologia, Ospedale Policlinico San Matteo, 27100-Pavia, Italy
Eur J Cancer Clin Oncol; 18(3):237-242 1982

We reviewed 251 consecutive adult patients with Hodgkin's disease treated at the Division of Hematology, Policlino San Matteo, Pavia, from January 1970 to December 1979, to assess the risk of development of acute leukemia. The median time of follow-up was 48 mo (range 6-135). No leukemia occurred in 88 patients treated with radiotherapy or chemotherapy alone. Six acute non-lymphoid leukemias occurred in the group of 163 patients treated with MOPP and radiotherapy (crude rate of leukemia of 7.5 per 100 person-yr at risk). All cases were in clinical remission and off-therapy; the latent period from initiation of therapy to onset of leukemia ranged between 30 and 90 mo. The actuarial probability of leukemia at 5 and 7 yr was 2.9 and 4.7% for the entire group of patients, and 3.8 and 5.8% for the combination therapy group. All leukemias, except one, had a preleukemic phase lasting 1-12 mo, with cytopenia and dysplastic marrow. The median survival after leukemia was 4.7 mo. (Author abstract) (19 Refs)

9. LEUKEMIA IN BENZENE WORKERS.

Rinsky RA, Young RJ, Smith AB
Natl. Inst. Occupational Safety and Health Centers for Disease Control, Cincinnati, OH, 45226
Am J Industr Med; 2(3):217-245 1981

A report based upon 98% vital status follow-up of a previously reported cohort mortality study of benzene-exposed workers is presented. Included are all available determinations of environmental benzene concentrations, the risk of leukemia experienced by a cohort of 748 workers exposed for at least 1 day to benzene between 1940 and 1949 (Group 1) and a cohort of 258 workers exposed between 1950 and 1959 (Group 2), leukemia risk in Group 2, and clinical information on all leukemia deaths. Mortality for all causes in Group 1 was only slightly greater than expected in the referent population of United States white males. Mortality for lymphatic and hematopoietic malignancies, however, showed a large, significant increase over the expected mortality [standardized mortality ratio (SMR) = 330]. Seven deaths were from leukemia (SMR = 560); for workers exposed for greater than 5 yr, the SMR for leukemia was 2,100. All leukemias were myelogenous or monocytic. In Group 2, the overall death rate was lower than expected, probably because of the young age of the workers. One case of leukemia was observed vs 0.46 expected (SMR = 217). The 8-hr time-weighted av benzene exposures of these workers were within recommended standards in effect at the time of exposure. (37 Refs)

10. NEUROLOGICAL ABNORMALITIES IN CHRONIC BENZENE POISONING. A STUDY OF SIX PATIENTS WITH APLASTIC ANEMIA AND TWO WITH PRELEUKEMIA.

Baslo A, Aksoy M
Section Hematology, Internal Clinic, Capa, Istanbul
Environ Res; 27(2):457-465 1982

Neurological, electromyographical and motor conduction velocity examinations were applied to six patients with aplastic anemia and two cases of preleukemia due to chronic exposure to benzene. In addition, sensory conduction velocities were measured in three patients. Neurological abnormalities were found in four out of six pancytopenic individuals. There was a certain relationship between the presence of neurological abnormalities and the period of cessation of the exposure. In the two patients with preleukemia similar neurologic abnormalities were found. (Author abstract) (13 Refs)

11. MALIGNANT LYMPHOMA IN FIRST-DEGREE BLOOD RELATIVES.

Haim N, Cohen Y, Robinson E
Dept. Oncology, Rambam Medical Center, Haifa, Israel
Cancer; 49(10):2197-2200 1982

The statistical significance of familial lymphoma in first-degree blood relatives was evaluated for the series of all lymphoma cases referred to our department since 1968. Four pairs of immediate relatives with Hodgkin's disease (HD) were found among 183 patients diagnosed between 1960 and 1980. The expected number during that period was 0.45. Thus, close relatives of HD patients had about ninefold increased risk of the disease (p less than 0.005). Mixed-cellularity was the most common subtype in these familial cases (6/8 patients). There were three pairs of close relatives with non-Hodgkin's lymphoma (NHL) among 532 patients diagnosed during the same period, 1960-1980. The expected number was 3.86. These findings further indicate that HD may differ from NHL with regard to familial clustering. (Author abstract) (30 Refs)

EPIDEMIOLOGY AND ETIOLOGY OF NON-HUMAN LEUKEMIA AND LYMPHOMA

12. THE PATHOGENESIS OF PLASMA CELL TUMORS.

Hollander VP, Platica M
Res. Inst., Hospital for Joint Diseases, New York, NY, 10035
The Handbook of Cancer Immunology Volume 6: Lymphoid Cell Subpopulations-Structure, Function, and Interactions. Waters H, ed. New York, Garland STPM Press, 314 pp., 1981.

The possibility is examined that common factors are at play in the mineral-oil induced plasma cell tumors (PCT) in BALB/c mice because so many endocrine factors appear to modulate tumorigenesis. The working hypothesis involves bacterial lipopolysaccharide in a transformation step, pristane-induced peritoneal factors in the successful adaptation of nascent tumor cells to the host, and finally, an immunosuppression step which permits rapid growth. Hormones are involved in the earlier steps of plasmacytoma development. (145 Refs)

13. AN EPIZOOTIC OF LYMPHOMA IN NORTHERN PIKE, ESOX LUCIUS L., FROM THE ALAND ISLANDS OF FINLAND.

Thompson JS
Dept. Virology, Univ. Helsinki, Haartmaninkatu 3, 00290 Helsinki 29, Finland
J Fish Dis; 5(1):1-11 1982

An epizootic of lymphoma in northern pike is described. Nineteen saltwater pike (17 male, 2 female), had 1-8 dermoid tumors each, distributed from snout to tail fin. Tumor size av 2.3 cm (range 0.5-6.0 cm). Some of the tumors were invasive to underlying muscle, but none had metastasized. Thirteen fish had multiple tumors. Light microscopy revealed undifferentiated mononuclear cells, lack of mitoses (the few present were pathological), and multinucleated giant cells. The morphology was suggestive of stem cells (hemocytoblasts) or lymphoblasts. Kidney, liver, and spleen cells were normal. Electron microscopy (EM) revealed lymphoblast-like cells, and in one pike, two electron-dense particles suggestive of intercellular retroviruses. Tumor cell cultures survived longer at 4 C than at 20 C. Multinucleated giant cells and pathological mitoses were seen in a 4 C culture. Sodium butyrate treatment did not induce further differentiation than that inherent at 4 C. EM did not reveal viral particles in cultured cells, but retrovirus-like particles were seen in the supernatants. Treatment of the cell cultures with 5-bromodeoxyuridine did not induce EM-detectable virus production. The findings are compared with reports of pike lymphoma from other locations. (29 Refs)

14. EVIDENCE FOR THE HORIZONTAL ACQUISITION OF MURINE AKR VIROGENES BY RECENT HORIZONTAL INFECTION OF THE GERM LINE.

O'Brien SJ, Moore JL, Martin MA, Womack JE
Lab. Viral Carcinogenesis, NCI, NIH, Frederick, MD, 21701
J Exp Med; 155(4):1120-1132 1982

Estimations of the genetic distance based on 51 randomly selected biochemical loci between Mus musculus molossinus, AKR, C58, NIH Swiss, and 12 12 other mouse strains were performed in order to determine the origin of murine AKR virogenes. By comparing the composite allozyme genotype of various inbred and outbred mouse strains, the genetic distance statistic was derived. The genetic distance measures the degree of allelic substitution between populations and increases proportionally with the amount of time the populations have been reproductively isolated. The genetic distance determined between molossinus and all the inbred strains, including the virus-positive strains was significantly larger (3-20x) than any of the measurements between consanguinity of the strains. Restriction enzyme digestion of liver DNA from molossinus, AKR, and inbred strains that express ecotropic murine leukemia virus was used to analyze cellular DNA sequences that flank the integrated AKV provirus. Molossinus cell DNA did not contain the integration flanks of three AKR provirus sequences, while it contained at least six different proviral integration fragments. These results are most easily explained by a recent germ line infection of a progenitor of AKR by a molossinus virus, and exclude the interpretation of consanguinity of AKR and molossinus. (47 Refs)

15. GENETIC INTERACTIONS IN INDUCTION OF ENDOGENOUS MURINE LEUKEMIA VIRUS FROM LOW LEUKEMIC MICE.

McCubrey J, Risser R
McArdle Lab. Cancer Res., Univ. Wisconsin, Madison, WI, 53706
Cell; 28(4):881-888 1982

The frequency of ecotropic murine leukemia virus (MuLV) production in cells induced with halogenated pyrimidines has been investigated in several low leukemic strains of mice. Very few BALB/c or C57BL/6 (B6) induced embryo cells produce MuLV; this low frequency increases 10 to 50 fold in cells of the BALB/c x B6 F1 hybrid. Data from backcrosses of the F1 hybrid to each parent and from BALB/c x B6 recombinant inbred strains indicate that the phenotype of enhanced MuLV production results from interaction of two unlinked loci, dominant (+/+ τεστσ ωιτη ΒΑΛΒ/γ χ Β∉ ρεγομβιναντ ινβρεδ σ τραιν) confirm this two-locus model. The loci are designated Inc-1 and Inb-1 to signify their phenotypic detection by induction and the BALB/c or B6 strain of origin, respectively. Examination of hybrids of BALB/c and of B6 with other strains indicates that strains related in pedigree to BALB/c carry Inc-1, whereas those related to B6 carry Inb-1. Identification of genetic loci that specifically interact to enhance MuLV production after exposure to halogenated pyrimidines indicates the existence of mechanisms that regulate the induction or intracellular expression of endogenous MuLV. (Author abstract) (31 Refs)

CYTOGENETIC AND MORPHOLOGIC STUDIES

16. FREQUENCY OF PHILADELPHIA CHROMOSOME AND OTHER CHROMOSOMAL CHANGES IN ADULTS WITH CHRONIC GRANULOCYTIC LEUKEMIA.

Zapata-Gayon N, Arechavala-Perichard E, Pizzuto J, Cea-Cerros GA, Gonzalez-Angulo A
(c/o Gonzalez-Angulo) Apartado Postal 73-032, Mexico, D.F., Mexico
Arch Invest Med (Mex); 13(1):33-36 1982

Frequency of Philadelphia chromosome (PhC) and other chromosomal changes were studied in 74 patients (34 men, 40 women; 10-90 yr old) with chronic granulocytic leukemia. All the patients except one had the PhC, which was observed in all examined cells of the 63 patients and in 25-80% of examined cells of the 11 patients. Other chromosomal changes were noted in 20 patients; 8 had aneuploidy (AN), 1 had duplication of PhC (DPhC), 1 had the DPhC and a different modal number (49:XY), 3 had DPhC and AN, 2 had DPhC and polyploidy (PP), 1 had deletion, 1 had translocation and AN, and 3 had AN and PP. No correlation was evident between the chromosomal changes and survival. Longest survival was 11 yr observed in a 37 yr old woman with PhC in 100% of examined cells. Shortest survival was 40 days observed in a 22 yr old woman, who also had PhC in 100% of examined cells. Thirteen of the patients were lost, 14 died within 12 mo, 38 died within 12-72 mo, and 9 died within 72-132 mo. Majority of the patients died in blastic phase. (12 Refs) (In SPA)

17. A PHOTOMETRIC STUDY OF THE STANDARD PHILADELPHIA (PH(1)) TRANSLOCATION OF CHRONIC MYELOID LEUKEMIA (CML).

Wayne AW, Sharp JC
Dept. Haematology, King's Coll. Hosp., Denmark Hill, London SE5 8RX, England
Cancer Genet Cytogenet; 5(3):253-256 1982

A newly developed form of high resolution microscope photometry has been employed in a study of the relationships between the chromosomes involved in the standard Philadelphia (Ph(1)) translocation of chronic myeloid leukemia (CML). The intention of the investigation was to provide quantitative data on the relative amount of material exchanged between the No 9 and No 22 chromosomes. A marked consistency in the amount of material lost from the Ph1 was observed, and the balanced nature of the standard Ph1 translocation was confirmed. The data are also in accordance with the concept of a reciprocal exchange between the No 9 and No 22 chromosomes. (Author abstract) (9 Refs)

18. VARIANT PH1 TRANSLOCATIONS IN CML AND THEIR INCIDENCE, INCLUDING TWO CASES WITH SEQUENTIAL LYMPHOID AND MYELOID CRISIS.

Oshimura M, Otyashiki K, Terada H, Takaku F, Tonomura A
Dept. Cytogenetics, Medical Res. Inst., Tokyo Medical and Dental Univ., Tokyo 113, Japan
Cancer Genet Cytogenet; 5(3):187-201 1982

A serial cytogenetic study of 110 cases of chronic myelogenous leukemia (CML) has been performed with G- and/or Q-banding techniques with the following results. (1) Seven out of the 110 cases were karyotypically normal. (2) A variant Ph1 translocation was observed in three cases. (3) The frequency of Ph(1)-negative CML and that of Ph(1)-positive CML with various types of Ph1 translocation from 15 studies reported as series of 25 or more cases, including the present study, have been tabulated. The incidence of a variant Ph1 translocation was 4.1%. (4) In one case of the present study, a masked Ph1 by a translocation of material onto the short arm of the 22q- was observed in the blastic crisis but not in the chronic phase. From the present study and a review of the published cases, it appears that the incidence of such a 'masked' Ph1, which cannot be detected by conventional Giemsa staining, is less than 0.6% in CML cases. (5) The first and the second cases with a variant Ph1 translocation mentioned above developed a myeloid blastic crisis after the induction of remission of a lymphoid blastic crisis. For the present, it is unclear whether the occurrence of such blast cells in the two cases and the cytogenic findings are coincidental. However, the evidence supports the notion of 'lymphoid-myeloid' multipotentiality of certain leukemic cells. (32 Refs)

19. Y CHROMOSOME DUPLICATION IN CHRONIC MYELOID LEUKEMIA.

Stoll C, Oberling F
Institut de Puericulture, CHU, 23, rue de la Porte de l'Hopital, F-67000 Strasbourg, France
Nouv Rev Fr Hematol; 24(1):9-12 1982

Karyotypic analysis of bone marrow and blood obtained during the acute phase of chronic myeloid leukemia (CML) was performed in an adult male. Duplication of the Y chromosome was found in addition to some other abnormalities. While a less favorable prognosis has been suggested for those with Y duplication vs those with missing Y, the 6 mo survival in the present patient and a mean 3.5 mo survival in other patients

with CML in blastic crisis prevent any conclusions with respect to an unfavorable role for Y duplication in CML. (16 Refs)

20. ACUTE MONOCYTIC LEUKEMIA CHROMOSOME STUDIES.

Berger R, Bernheim A, Sigaux F, Daniel MT, Valensi F, Flandrin G
Laboratoire de Cytogenetique, Centre G. Hayem, Paris Cedex 10, France
Leuk Res; 6(1):17-26 1982

Bone marrow cells from 10 children and 24 adults with acute monocytic leukemia (24 poorly differentiated [M5a], 10 well differentiated [M5b]), were subject to cytogenetic analysis directly or after culturing without stimulation. All of the studies were performed at diagnosis, prior to treatment. Analysis consisted of G- and R-banding, and sometimes C- and Q-banding, and also cytologic identification of cells. Two patients had constitutional chromosomal abnormalities. Twelve patients (5 M5a, 7 M5b) had no abnormalities. All the remaining patients had numerical, structural, or combined abnormalities. Five patients had autosomal trisomies involving chromosomes 8, 9, 21, and 12 (?), which were also associated with structural abnormalities in another six. Twelve of the patients, mostly M5a, had structural rearrangement of chromosome 11 (at bands q22-q24 in 9, q14 in 3). Two different abnormal cell lines were seen in two patients, one at diagnosis and one at relapse. Cytologic study showed that most mitoses were seen in monocytes or monoblasts. Findings are discussed and compared to cytogenetic findings in other leukemias. (19 Refs)

21. THE ROLE OF COMPLEMENT IN THE FUNCTION OF THE MONOCYTE-MACROPHAGE SYSTEM.

Schmalzl F
Univ. Klinik fur Innere Medizin, Anichstrasse 35, 6020 Innsbruck, Austria
Haematol Blood Transfus; 27:145-156 1981

Cytological and functional characterization of leukemic monocytes in 42 cases of monocytic leukemia (24 mature, 18 immature) and 12 cases of 'myelomonocytic' leukemia is reviewed. Thirty cases from other sources were also studied. The monocytic character of the leukemic population can be suggested by morphology, lysosomal enzymes, lysozyme determinations, production of colony-stimulating activity, surface receptor (IgG, complement), glass adherence, and perhaps type of growth in agar culture and phagocytosis; and strongly suggested by ultrastructure, cytochemistry, transformation into macrophages, migration into inflammatory exudates, and perhaps by monocyte-specific antibodies. Proven confirmation can occur only with a combination of several of the above tests; a combination of cytochemical and/or ultrastructural examination with functional tests is recommended. The myelomonocytic type of monocytic leukemia is characterized by the presence of monocytic and granulocytic differentiation at the same time, while the monocytic type has almost exclusively monocytic or monoblastic differentiation of leukemic cells. The specific cytologic properties of leukemic monocytes may induce peculiar clinical features. Quantitative differences in the expression of functional properties and cytological features may depend on the varying degree of maturation of the leukemic disorder and may be important for the clinical course. Monocytic leukemias should be considered separate clinical entities among the acute leukemias. (65 Refs)

22. LYSOSOMAL GRANULES IN LEUKEMIC MONOCYTES AND THEIR RELATION TO MATURATION STAGES.

Catovsky D, O'Brien M
MRC Pathology, Hammersmith Hosp., Royal Postgraduate Medical Sch., Ducane Road, London W12 OHS, England
Haematol Blood Transfus; 27:167-173 1981

Bone marrow and/or peripheral blood cells from 11 patients with monocytic leukemia were studied with light and transmission electron microscopy (TEM) cytochemical techniques. Two of the patients had monoblastic transformation of chronic granulocytic leukemia. Seven patients had poorly differentiated and four had differentiated leukemia. Cytochemical reactions for myeloperoxidase (MPO), Sudan Black B, acid phosphatase (AP), naphthol-AS acetate esterase, and alpha naphthyl acetate esterase were performed. TEM was used to examine cell morphology and for evaluation and localization of MPO and AP activity. Conventional TEM in two cases revealed typical ribosome-lamella complexes. AP and MPO reactions at the TEM level revealed three types of lysosomal granules: primary granules were the smallest in size, were mainly seen in monoblasts and were characteristically AP positive; secondary granules were seen from the promonocyte stage onwards, were of medium size, were MPO positive with some AP activity, and persisted, but in smaller numbers, with maturation; tertiary granules were of variable size and were negative for AP and MPO. These results demonstrated the sequential development of lysosomal enzymes during monocytic differentiation. (7 Refs)

23. THE BIOCHEMICAL AND GENETIC BASIS FOR THE MICROHETEROGENEITY OF HUMAN R-TYPE VITAMIN B12 BINDING PROTEINS.

Yang SY, Coleman PS, Dupont B
Dept. Immunogenetics, Sydney Farber Cancer Res. Inst., 44 Binney St., Boston, MA, 02115
Blood; 59(4):747-755 1982

R-type vitamin B12 binding proteins (R proteins) from human granulocytes, erythrocytes, plasma, and other body fluids were characterized by isoprotein banding patterns on autoradiograms after resolution via thin-layer polyacrylamide isoelectric focusing (IEF) gel electrophoresis. R proteins obtained from various tissue sources in a given individual show tissue-specific electrophoretic patterns. The desialated R proteins obtained following in vitro treatment with neuraminidase are, however, the same for any given individual and do not show tissue specificity. The differences seen in native R proteins (ie, transcobalamin (TC) I, III, and others) obtained from different tissues are due to variations only in the sialic acid content. Granulocytes from patients with chronic myelogenous leukemia (CML) contain both TC I and TC III, and these R proteins can be released in vitro by lithium stimulation. Normal granulocytes contain only TC III. Differences in desialated R proteins from individual to individual are due to a genetic polymorphism controlled by a single genetic locus (designated TCR) with two alleles, 1 and 2, which are found to be codominantly expressed in heterozygous individuals. The allelic variants of the desialated R proteins found in different blood cells and body fluids are controlled by only one genetic locus. (Author abstract) (34 Refs)

24. REARRANGEMENT OF CHROMOSOME NO. 3 IN A CASE OF PRELEUKEMIA WITH THROMBOCYTOSIS.

Norrby A, Ridell B, Swolin B, Westin J
(c/o Westin) Dept. Medicine, Ostra Hosp., S-416 85 Goteborg, Sweden
Cancer Genet Cytogenet; 5(3):257-263 1982

The clinical and cytogenetic findings of a patient with the preleukemic syndrome and a structural rearrangement involving both chromosomes No 3 are described. The karyotypic abnormality consisted of an insertion of a part of the long arm of one chromosome No 3 into the other, ie, ins(3;3)(q27;q21q27). A prominent feature of the bone marrow was a marked megakaryocytic hyperplasia. The platelet count temporarily exceeded 1,000 x 10(9)/liter. The findings of the present case, together with similar observations by others, suggest that the long arm of chromosome No 3 may contain a region involved in the regulation of megakaryopoiesis. (Author abstract) (15 Refs)

25. CYTOGENETICS OF PRELEUKEMIA.

Nowell PC
Dept. Pathology, Sch. Medicine, Univ. Pennsylvania, Philadelphia, PA, 19104
Cancer Genet Cytogenet; 5(3):265-278 1982

A summary is presented of the major cytogenetic findings in various hematopoietic disorders that carry an increased risk for leukemia, with emphasis on the more recent results with banding techniques. Groups of disorders discussed include cytopenic disorders (dysmyelopoietic syndromes, DS) (DS with specific chromosome changes, cytogenetic evolution and progression to leukemia, cytopenic preleukemia in patients previously treated for malignant disease, prognostic value of chromosome studies in cytopenic preleukemia); myeloproliferative disorders (MD) (prognostic value of chromosome studies in MD); and preleukemic disorders of childhood (clinical value of chromosome studies in childhood preleukemia). Biological significance of chromosome changes in preleukemia is considered. Some evidence suggests that chromosome studies may be of prognostic value in DS; patients with abnormalities show decreased survival time and are at increased risk for progression to ANLL (acute non-lymphocytic leukemia). Karyotypic findings in the preleukemias suggest that the various clinical disorders are a group of related diseases derived from an altered hemic stem cell. (61 Refs)

26. FOUR CASES OF FAMILIAL CHILDHOOD ACUTE LYMPHOCYTIC LEUKEMIA INCLUDING THREE CASES IN A SIBSHIP.

Tsunematsu Y, Koide R, Sasaki M, Utsumi J
Div. Hematology and Oncology, Natl. Children's Hosp., Tokyo, Japan
Rinsho Ketsueki; 22(12):1938-1947 1981

Four cases of familial childhood acute lymphocytic leukemia (ALL), including three cases in siblings, were studied. The fourth patient was a half cousin of the other three. The two families have had no contacts, and no specific environmental factors were noted. All four were in the same generation, and there were no marriages between the members of the family. Both families descended from a female who had two spouses, and the female's siblings all died within 8 yr of age. All siblings of the father of the three ALL cases also died in young ages, and one of them was suspected of having died of ALL. Two patients were examined by electron microscopy for C-type particles; none were found, nor were other inclusion bodies found. No reverse transcriptase was found in all patients. Pedigree analysis suggests that ALL cases were likely a result of a genetic mechanism with a dominant inheritance for genetic susceptibility. Immunogenetic examination revealed that the surviving patients and the obligate carriers had the same HLA haplotype, AW19 BW40. Chromsome analysis showed no chromosomal abnormality, but G-banding of skin fibroblast cells revealed chromosomal rearrangement in the patients and the obligate carriers. These two findings in cytogenetic and immunogenetic studies may be important as possible phenotypic markers for prediction of predisposition to leukemia. (35 Refs) (In JPN)

27. NEONATAL LEUKEMOID REACTION: AN ISOLATED MANIFESTATION OF MOSAIC TRISOMY 21.

Weinberg AG, Schiller G, Windmiller J
Univ. Texas Health Science Center at Dallas, Dallas, TX
Am J Dis Child; 136(4):310-311 1982

A phenotypically normal neonate with an unexplained leukemoid reaction had a 46,XX/47,XX, +21 karyotype limited to the hemopoietic system. Although a self-limited myeloproliferative syndrome occurs in Down's syndrome, this case confirms that an identical disorder may develop in patients with mosaic trisomy 21 and no phenotypic stigmas of Down's syndrome. Chromosome analysis is a necessary adjunct to the examination of any neonate with an unexplained leukemoid reaction. The presence of trisomy 21 should lead to conservative management, unless there is life-threatening progression of the disease. (Author abstract) (11 Refs)

28. HUMAN PLASMACYTOMA WITH AN UNUSUAL KARYOTYPE GROWING IN VITRO AND PRODUCING LIGHT-CHAIN IMMUNOGLOBULIN.

Karpas A, Fischer P, Swirsky D
Dept. Haematological Medicine, Cambridge Univ. Clinical Sch., Cambridge, England
Lancet; 1(8278):931-933 1982

A new human plasmacytoma line (Karpas 707) was established from the cells of the bone-marrow and peripheral blood of a patient with Bence-Jones-positive multiple myeloma. The cells of this new line resembled the patient's malignant cells and fresh myeloma cells from nine other patients in being Epstein-Barr viral nuclear antigen negative. They looked like plasma cells and they secreted only lambda light chains. Both these cells and the patient's fresh cells were hypodiploid and contained the Philadelphia chromosome and several other markers. This line seems to be the first human plasmacytoma line since the IgE lambda-producing line (U266) established in 1968, and it may be suitable for the production of human monoclonal antibodies. (Author abstract) (14 Refs)

29. EXTRA CHROMOSOME 12 AND PROGNOSIS IN CHRONIC LYMPHOCYTIC LEUKAEMIA.

Robert KH, Gahrton G, Friberg K, Zech L, Nilsson B
(c/o Gahrton) Section Clinical Hematology and Oncology, Dept. Medicine, Huddinge Hosp., S-141 86 Huddinge, Sweden
Scand J Haematol; 28(2):163-168 1982

Peripheral blood lymphocytes from 22 consecutive patients with chronic lymphocytic leukemia were stimulated with the polyclonal B-cell mitogens lipopolysaccharide from E coli (LPS) and Epstein-Barr virus (EBV). Stimulation was successful for chromosome analysis in 14 patients. Eleven patients had chromosomal aberrations and 7 of these had an extra chromosome 12. In two patients an extra chromosome 12 was the only abnormality, while additional aberrations were found in five patients. Three patients had complex aberrations involving de-

letion of chromosome 6. One of these patients also had a translocation between chromosomes 12 and 14. One patient had a translocation between chromosomes 11 and 14. In three patients no aberrations were detected. The time elapsing between diagnosis and appearance of clinical symptoms which were indications for treatment was significantly shorter in patients with an extra chromosome 12 than in those without this abnormality. Thus, it appears that an extra chromosome 12 is associated with a more rapid course of the disease, and may therefore be of importance for the prediction of prognosis. (Author abstract) (10 Refs)

30. PATIENT WITH ACUTE B-CELL LEUKEMIA OF BURKITT'S TYPE (L3) AND MARKER CHROMOSOMES INCLUDING AN (8;14) TRANSLOCATION.

Roos G, Nordenson I, Osterman B, Jorpes P, Rudolphi O
Dept. Pathology, Univ. Umea, S-901 87 Umea, Sweden
Leuk Res; 6(1):27-31 1982

Bone marrow cells from a 20-yr-old man with B-cell acute lymphocytic leukemia (B-ALL) of Burkitt's type (L3) were analyzed morphologically, cytogenetically, and for surface markers. Recurrent jaw involvement was noted. Three remissions were achieved after chemo- and radiotherapy, with bone marrow and CNS relapses each time. The patient died 7 mo after diagnosis. Tumor cells were large and homogeneous in size, and corresponded to ALL, type L3. Cells isolated in partial remission after 6 mo of treatment were 20% blasts and 50% lymphocytes; 40% formed rosettes with sheep RBC, and 28% (mainly blasts) were monoclonal B cells (IgM, lambda). The cells had typical L3 morphology and a similar monoclonal immunoglobulin pattern. Karyotypes were normal of 10 and 5 cells in remissions. However, in a following relapse abnormalities were seen: 46,XY,dup(1)(q21;q32),del(6)(q23),t(8;14)(q23;q32) in seven cells; the same abnormalities with an additional chromosome 9 in two cells; and 46,XY,dup(1)(q21;q32),del(6)(q23) in one cell. Similarities between Burkitt's lymphoma and B-ALL type L3 are discussed. (8 Refs)

31. NONCUTANEOUS PERIPHERAL T-CELL LYMPHOMA HISTOLOGICALLY RESEMBLING MYCOSIS FUNGOIDES.

Weisenburger DD, Nathwani BN, Forman SJ, Rappaport H
Dept. Pathology, Mercy San Juan Hosp., 6501 Coyle Ave., Carmichael, CA, 95608
Cancer; 49(9):1839-1847 1982

We have studied the clinical and pathologic features of three patients with a distinctive non-Hodgkin's lymphoma of the diffuse mixed cell type. The tumors were characterized by a mixture of lymphoid cells of widely varying size and degree of nuclear transformation. A distinctive feature of the neoplastic cells was the presence of cerebriform nuclear contours identical to those seen in mycosis fungoides. Immunologic studies performed on lymph nodes from two patients revealed that the neoplastic cells were T-cells. Characteristic clinical features of the patients were an advanced stage of disease at diagnosis, absence of skin lesions, presence of lung involvement, poor response to aggressive chemotherapy, and a short survival time (9-13 mo). The features described closely resemble those of the pleomorphic variant of Japanes adult T-cell leukemia-lymphoma. (Author abstract) (44 Refs)

32. CHRONIC T-CELL LEUKEMIAS II. CYTOGENETIC STUDIES.

Pittman S, Morilla R, Catovsky D
(c/o Catovsky) MRC Leukaemia Unit, Royal Postgraduate Medical Sch., DuCane Road, London W12 OHS, England
Leuk Res; 6(1):33-42 1982

Peripheral blood lymphocytes from 10 patients (7 males, 3 females; 12-76 yr old) with chronic T-cell leukemias (3 chronic lymphocytic leukemia [CLL], 6 prolymphocytic leukemia [PLL], 1 lymphosarcoma cell leukemia) were studied cytogenetically after phytohemagglutinin (PHA) stimulation. Structural and numerical abnormalities were seen in some cells from all cases, but these were consistently clonal only in the PLL patients. The most common numerical abnormality was hypodiploidy, seen in five cases, more frequently involving loss of chromosomes 8 or 9 than others. Chromosomes most frequently involved in marker formation were 2 and 8, with a lesser frequency with 7, 9, 11, and 16. Structural rearrangements were seen in only 3/8 cases with abnormal number 8 chromosomes. No abnormalities of chromosome 14 were seen. Chromosome 2 may contain information about control of T cell proliferation, since it is often abnormal in T cell neoplasias. It is suggested that the differences in chromosomal abnormalities reported may be related to the different proliferative behavior of CLL and PLL. (22 Refs)

33. HYPOTONIC DESTRUCTION UNCOVERS CHROMOSOMAL ABERRATION.

Schroder J, Grunewald B, Struck L
Institut fur Rechtsmedizin der Universitat, D-2000 Hamburg, W. Germany
Naturwissenschaften; 69(3):150 1982

Nuclei with appendages resembling drumsticks or micronuclei were discovered following hypotonic treatment of leukemic WBC in mature and immature myeloid cells from 3/5 patients with acute myeloid leukemia. The results suggested that the appendage may represent a supernumerary chromosome inactivated during interphase. Screening for nuclei with appendages following hypotonic treatment may possibly be useful in determining cell lines with certain types of chromosomal changes. (4 Refs)

34. HOW DO HUMAN ISOCHROMOSOMES ARISE?

de la Chapelle A
Dept. Medical Genetics, Univ. Helsinki, Haartmaninkatu 3, 00290 Helsinki 29, Finland
Cancer Genet Cytogenet; 5(2):173-179 1982

Characteristics of isochromosomes (IC), metacentric elements formed by transverse instead of longitudinal division of the the centromere, are reviewed. Both constitutional and acquired isochromosomes are described. IC are not uncommon in human leukemias and tumors. The best-known example, i(17q), occurs not only in the blastic phase of chronic myeloid leukemia, but also in many other leukemias and tumors. In contrast to congenital abnormalities, many chromosome arms may be found as IC in cancer cells. Descriptions of IC of 1q, 1p, 2p, 5p, 7q, 11q, and 16q have been found in addition to 17q. In lymphoma i(8q) and i(6p) have recently been observed. The role of misdivision of the centromere in the development of IC is discussed. The nonrandom occurrence of the various acquired IC within the karyotype may be because IC are formed with nonrandom frequency or because they lead to different consequences (selective advantage or disadvantage). Observations and interpretations are presented. (27 Refs)

BIOCHEMICAL, IMMUNOLOGICAL AND OTHER CELL BIOLOGY STUDIES

35. 'TARGET' CELLS, CELLULAR PHENOTYPES, AND LINEAGE FIDELITY IN HUMAN LEUKAEMIA.

Greaves MF
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J Cell Physiol; Suppl1:113-125 1982

Features of leukemic phenotypes in relation to normal hemopoietic differentiation were investigated in a study developed as a part of a routine immunodiagnostic service for leukemia in the United Kingdom (UK). Leukemic samples (heparinized blood, lymph node biopsies, cerebrospinal fluid, and peritoneal aspirates) were obtained from referring hospitals throughout the UK. A presumptive normal sequence of antigen (and other marker) expression in T cell differentiation is presented. The scheme is based upon reported antigenic heterogeneity of cortical and medullary thymocytes and subsets of blood T cells. The corresponding maturation 'positions' of 95 leukemic T cell phenotypes analyzed are presented. T-acute lymphoblastic leukemia (T-ALL), and T-non-Hodgkin's lymphoma in childhood 'correspond' to early or late thymocyte populations while T cell leukemias or lymphomas of older (greater than 35 yr) patients diagnosed as cutaneous lymphoma or leukemia, chronic lymphocytic leukemia, prolymphoblastic leukemia, or lymphoblastic lymphoma, all had 'mature' T phenotypes. The phenotypes that were documented in non-T-ALL are summarized. The majority of complementary ALL that do not synthesize detectable mu chain nevertheless have rearranged mu chain genes as revealed by molecular hybridization studies. Alterations in phenotype during leukemia progression or relapse may provide some evidence for distortion of 'normal' genetic programs as well as revealing the lineage affiliations of various clonogenic populations. Alterations in the latter population may indirectly indicate the possible target cell population involved. (89 Refs)

36. CELL LINEAGES IN HEMATOPOIETIC NEOPLASIA STUDIED WITH GLUCOSE-6-PHOSPHATE DEHYDROGENASE CELL MARKERS.

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J Cell Physiol; Suppl1:37-43 1982

The indirect method based upon study of hematologic neoplasms arising in females whose X-chromosomes inactivation mosaicism is delineated with glucose-6-phosphate dehydrogenase (G6PD) markers is reviewed. Chronic myelogenous leukemia (CML), lymphocytes in CML, significance of Philadelphia chromosome (Ph), agnogenic myeloid metaplasia with myelofibrosis, other myeloproliferative disorders, acute nonlymphocytic leukemia (ANLL), chronic lymphocytic leukemia, applications of the G6PD system to the study of hematologic cell regulation in neoplasia, and potential applications of the G6PD system to the study of long-term hematologic cell cultures are discussed. Several types of investigations indicate that cells of CML clone differentiate into B-lymphocytes. The G6PD findings in lymphocytes in patients with CML indicate the existence of similar stem cells to those in rodents and that CML involves a stem cell pluripotent for lymphocytes as well as for myelogenous cells. Studies of G6PD and chromosomes in B-lymphoblastoid cell lines established from a patient with Ph-positive leukemia who was heterozygous for G6PD provide evidence for the existence of cells derived from the abnormal clone that are Ph-negative. Thus, acquisition of Ph may not be sufficient cause for the disease. Eight G6PD heterozygotes with ANLL have been studied. Only a single-enzyme G6PD phenotype was found in the leukemic blast cells, suggesting that the disorders in these patients were clonal. In the patients who were studied when their disease entered remission, a return to normal double-enzyme phenotype in granulocytic cells was observed. (47 Refs)

37. SOLUBLE CYTOSTATIC FACTOR(S) RELEASED FROM HUMAN MONOCYTES. I. PRODUCTION AND EFFECT ON NORMAL AND TRANSFORMED HUMAN TARGET CELLS.

Hammerstrom J
Section Haematology and Immunology, Dept. Medicine, Trondheim Regional Hosp., N-7000 Trondheim, Norway
Scand J Immunol; 15(3):311-318 1982

Human monocytes activated with lymphokines after 3-7 days of in vitro maturation released stable cytostatic factor(s) (CF), as determined by reduction of [methyl-3H]thymidine incorporation and cell counts in target cell cultures. Lipopolysaccharide from Escherichia coli slightly enhanced the release of CF. The CF release was greatest at an intermediate stage of the in vitro monocyte maturation to large, macrophage-like cells. Three transformed human cell lines (NHIK 3025, K-562, and U-20S) and normal skin fibroblasts were consistently inhibited by CF. Normal human mesothelial cells were variably affected, while normal human lymphocytes proliferating in response to allogeneic cells in mixed lymphocyte culture were not inhibited. Further analysis of CF may disclose one of the mechanisms whereby human monocytes and macrophages inhibit growth of human tumor cells. (Author abstract) (34 Refs)

38. STUDIES ON ANTIGENS OF A LEUKEMIC NULL-CELL LINE (NALL-1). I. STIMULATORY CAPACITY IN MIXED LYMPHOCYTE CULTURE.

Uno J
Second Dept. Internal Medicine, Okayama Univ. Medical Sch., Okayama, Japan
Okayama Igakkai Zasshi; 93(5/6):481-487 1981

A one-way mixed lymphocyte reaction between lymphocytes from normal human donors and mitomycin C-treated cells from a human leukemic null-cell line (NALL-1) was investigated. Human leukemic T-cell and B-cell lines, an Epstein-Barr virus (EBV)-negative Japanese Burkitt's lymphoma line, and two EBV-positive normal B-cell lines were studied in parallel. Normal lymphocytes were stimulated significantly by the cultured null- and B-cells but not by the cultured T-cells. The stimulatory capacity of this null-cell line was approx equal to that of the leukemic, lymphoma, and normal B-cell lines, and was unrelated to the presence of complement receptor, surface immunoglobulin, EBV-associated nuclear antigen, terminal deoxynucleotidyl transferase or the origin of the cell lines. These results suggest that not only leukemic B-cells but also leukemic null-cells have stimulatory determinants in mixed lymphocyte culture. (Author abstract) (21 Refs) (In JPN)

39. CHARACTERIZATION OF TRANSFORMED CELLS AND TUMORS BY PROTON NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY.

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Cancer Res; 42(6):2270-2276 1982

Cultured acute lymphoblastic leukemic cells give a well-resolved proton nuclear magnetic resonance spectrum characteristic of isolated plasma membranes. We demonstrate that the signals, in the spectrum of whole cells, arise predominantly from the plasma membrane and that cells transformed by pokeweed mitogen have membranes which are significantly less rigid than are normal human peripheral blood lymphocytes. Normal thymus, malignant thymus, and a leukemic T-cell line have been compared by proton nuclear magnetic resonance spin echo experiments, and the normal thymus was found to differ. Cells transformed by the Epstein-Barr virus can also be characterized and shown to differ from the leukemically transformed cells by spin echo experiments. Since no probe molecule was required to obtain these results, this is the first definitive evidence that the structure and fluidity of the plasma membranes change as a result of transformation of lymphocytes. Proton nuclear magnetic resonance spectroscopy can now be used to compare the effect of different mitogens on T- and B-lymphocytes as well as to monitor the effects of drugs, metals, etc, on the plasma membrane of transformed lymphocytes. (Author abstract) (29 Refs)

40. A HUMAN PLASMA CELL LINE: INDUCTION AND CHARACTERIZATION.

Miller CH, Carbonell A, Peng R, Paglieroni T, MacKenzie MR
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Cancer; 49(10):2091-2096 1982

A stable line of IgG K producing human plasma cells was established from a myelomatous human bone marrow using conditioned media from a rapidly metabolizing lymphoblast line, RPMI 4098. Growth in RPMI 1640 (15% fetal calf serum) at 6% CO2 promoted a 62-hr doubling time with a preferred cell concentration of 1 x 10(6)/mL. Surface marker studies showed: no receptors for sheep erythrocytes, no surface immunoglobulins, variable number of cells bearing complement receptors and 83% bearing Fc receptors. Although transmission electron micrographs demonstrated a poorly developed endoplasmic reticulum, radioimmunoassay showed 23 ng IgG and 28.7 ng Kappa were produced by 1 x 10(6) cells in 72 hr. Further, the cells are lipase, esterase and Epstein-Barr nuclear antigen negative. ASG banding showed a total chromosome number that varied from 46-49. Since the number of human plasma cell lines is limited, it is felt that this line will augment the immunobiological study of human myeloma. (Author abstract) (16 Refs)

41. G-CSF: ITS RELATIONSHIP TO LEUKEMIA DIFFERENTIATION-INDUCING ACTIVITY AND OTHER HEMOPOIETIC REGULATORS.

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J Cell Physiol; Suppl1:53-64 1982

The interrelationship of the various factors produced by WEHI-3 leukemic cells was investigated with particular emphasis on the neutrophil-granulocyte colony-stimulating factor (G-CSF) activity and its relationship to leukemia differentiation-inducing activities induced by endotoxin in mouse and human sera. After stepwise column chromatography of WEHI-3D- conditioned medium (CM), the breakthrough fraction stimulated predominantly neutrophil-granulocyte colony formation, whereas the fraction eluted with 1 M NaCl induced primarily macrophage colony growth. The unseparated but concentrated CM contained significant mast cell growth factors and was a more active source than concanavalin A-stimulated mouse spleen CM. Tumor necrosis factor (TNF) according to the present study, is biochemically and functionally distinct from differentiation-inducing protein (GM-DF). The apparent lack of species specificity of TNF and its selective ability to inhibit proliferation of transformed cells, including WEHI-3B, suggests that acquisition of in vivo sensitivity of TNF may prove an important marker of leukemic transformation. The ability of Corynebacterium parvum plus endotoxin to induce high serum levels of TNF and of GM-DF with similar kinetics points to the importance of synergism studies with various biological response modifiers since TNF inhibits leukemic cell clonal expansion by a direct antiproliferative action, whereas GM-DF inhibits leukemic cell self-renewal by promoting terminal differentiation. (43 Refs)

42. EFFECT OF VARIOUS IMMUNOREGULATORY SUBSTANCES ON THE GROWTH INHIBITORY ACTIVITY (GIA) OF HUMAN MONOCYTES AGAINST LYMPHOBLASTOID CELL LINES.

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Immunopharmacology; 4(2):105-113 1982

Environmental or disease-related factors that may influence levels of cytostatic activity were studied and pharmacological manipulations were performed in an attempt to elucidate mechanisms involved in monocyte-tumor reaction and regulation. Human monocytes from healthy individuals are able to inhibit the growth, in vitro, of certain transformed lines. The activity was augmented by phorbol-12-myristate-13-acetate, and to some extent, interferon, but was not measurably affected by superoxide dismutase, catalase, prostaglandins, or steroids. Growth inhibitory activity was manifested by highly purified monocyte populations, whether obtained by elutriation or by removal after adherence to plastic. (23 Refs)

43. ISOLATION AND CHARACTERIZATION OF GLYCOSPHINGOLIPIDS FROM HUMAN LEUKOCYTES. A UNIQUE GLYCOSPHINGOLIPID PATTERN IN A CASE OF ACUTE MYELOMONOBLASTIC LEUKEMIA.

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Biochim Biophys Acta; 711(1):166-175 1982

Neutral glycosphingolipids and gangliosides were isolated from the malignant cells of a patient with acute myelomonoblastic leukemia. Structural analyses were performed by gas-liquid chromatography and by high-performance liquid chromatography combined with enzymatic hydrolysis of glycosphingolipids using glycosidases. We found that, in contrast to normal leukocytes and chronic leukemia cells which have only a single tetraosylceramide species, these acute myelomonoblastic leukemia cells have approx equal amounts of both globo- and neolactotetraosylceramide. This is the first population of human leukocytes in which we found two families of neutral glycosphingolipids to be present. The ganglioside fraction was composed of appreciable quantities of both NeuAcalpha 2

leads to 3Galbeta1 leads to 4Glcbeta1 leads to 1Cer (GM3, hematoside) and NeuAcalpha2 leads to 3Galbeta1 leads to 4GlcNAcbeta1 leads to 3Galbeta1 leads to 4Glcbeta1 1Cer (sialoparagloboside). These cells did not have the 'leukocyte-specific' N-acetylneuraminosyllactotriaosylceramide found in normal human lymphocytes and neutrophils. These results are discussed in relation to normal leukocyte differentiation and acute leukemia. The present study also illustrates the usefulness of combining enzymatic degradation with high-performance liquid chromatography for glycosphingolipid structural determination. (Author abstract) (28 Refs)

44. TRANSFERRIN RECEPTORS IN TRANSFORMATION AND DIFFERENTIATION.

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Protides Biol Fluid Proc Colloq; 29:451-454 1981

Human promyelocytic leukemia HL-60 cells, Burkitt's lymphoma Daudi cells, and myelogenous leukemia K562 cells were grown with 1.25% dimethylsulfoxide (DMSO), 0.1% sodium n-butyrate (SnB), or 1 x 10(-6) retinoic acid (RA) for 4 days at 37 C, and transferrin receptors and growth were examined. HL-60 cells originally consisted of myeloblasts and promyelocytes and differentiated to metamyelocytes and banded neutrophils following induction; Daudi and K562 cells were unchanged. The indirect immunofluorescence test revealed that all three cell lines were strongly reactive for transferrin receptors, but HL-60 cells were weakly reactive after culture with DMSO, SnB, or RA; Daudi and K562 cells remained strongly reactive. Growth of HL-60 cells was strongly inhibited by all three agents, Daudi cells by SnB, and K562 cells by RA; K562 cells were barely affected by SnB. These findings indicate a role for transferrin receptors in differentiation and transformation: loss of receptor activity may be interpreted as being an index of change from immature to mature or from malignant to normal. (18 Refs)

45. HYBRID RESISTANCE AGAINST A NATURAL KILLER (NK) CELL-RESISTANT LYMPHOMA (YWA) IS MEDIATED BY A T CELL-DEPENDENT MECHANISM.

Gronberg A, Klein GO, Karre K, Kiessling R, Klein G
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Eur J Cancer Clin Oncol; 18(2):183-190 1982

Rejection of the Moloney virus-induced YAC lymphoma of strain A origin by semisyngeneic F1 hybrids has previously been shown to correlate with the levels of natural killer (NK) cell activity in the same F1 hybrids against this target cell line in vitro. In the present study, YAC and another Moloney virus-induced lymphoma, YWA, derived from the A congenic A-SW strain, were tested for F1 hybrid resistance after sc inoculation of small numbers of cells into syngeneic and semisyngeneic F1 mice. While YAC cells invariably grew progressively once they formed a palpable tumor, regression of YWA tumors was frequently observed in both susceptible and resistant genotypes. The hybrid resistance pattern for YAC and YWA differed in one important respect: outcross of the syngeneic host to the A-congenic A-BY strain introduced a strong H-2b-associated resistance factor against YWA, but not against YAC. Compared to YAC, which is highly NK-sensitive and rapidly eliminated from mice with high NK activity, YWA was insensitive to NK-mediated lysis in vitro and [125I]UdR-labeled YWA cells were not eliminated more efficiently from the highly resistant (A-SW x A-BY) F1 than from the parental strain in short-term (4-18 hr) in vivo rejection assays. It was therefore concluded that the H-2b-associated resistance against YWA was independent of NK cells or other rapidly acting effector mechanisms. Moreover, thymectomy, followed by irradiation and fetal liver reconstitution, completely abolished the resistance against YWA but left the resistance against YAC virtually intact. These data suggest that two lymphomas induced by the same agent can be rejected by different effectors. The NK-resistant YWA lymphoma is rejected by a T-dependent mechanism, while the resistance against the inoculation of the highly NK-sensitive YAC line is T-independent and, in all probability, mediated by NK cells. (Author abstract) (22 Refs)

46. NATURAL ANTI-LYMPHOMA ACTIVITY IN C57BL/6 MICE: TIME COURSE OF APPEARANCE AND NATURE OF CYTOTOXIC ANTIBODIES.

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Instituto de Immunologia y Biologia Microbiana, Velazquez 144, Madrid 6, Spain
Immunol Lett; 3(4):195-198 1981

The presence of cytotoxic antibodies in the sera of normal C57BL/6 mice was measured by the cytotoxicity test against syngeneic leukemic cells induced by endogenous radiation leukemia virus. Activity could be detected in sera from 5-14-mo-old mice. Study of the nature of the antibody response indicated the activity could be attributed mainly to IgM antibodies until the age of 10 mo, whereas in sera of 12-mo-old mice an increasing level of IgG-like antibodies was demonstrated. (16 Refs)

47. SPECIFICITY STUDIES OF CYTOLYTIC T LYMPHOCYTES DIRECTED AGAINST MURINE LEUKEMIA VIRUS-INDUCED TUMORS. ANALYSIS BY MONOCLONAL CYTOLYTIC T LYMPHOCYTES.

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J Exp Med; 155(4):1050-1062 1982

Specificities of cloned cytolytic T lymphocytes (CTL) were investigated for the analysis of CTL populations generated against murine leukemia viruses (MuLV) in H-2 congenic BALB/c (H-2d) and BALB.B (H-2b) mice. CTL elicited by immunization with syngeneic Friend or Gross MuLV-induced tumors in these mice were studied. Optimal conditions for proliferation and long-term culture of MuLV-specific CTL were determined. Ninety-two lymphocyte clones were assayed independently on a panel of 51Cr-labeled tumor target cells. Clones were then distributed into different groups according to their specificities. Most of the CTL clones (52-64%) attacked the tumor cell against which they were initially primed and not any of the other tumor cells assayed. Other clones were specific for the priming MuLV-induced antigen in apparent association with an H-2 public specificity shared between H-2b and H-2d antigens (5-16%); were specific for tumor cells induced by Gross, Rauscher, Friend, and Moloney MuLV and were H-2 restricted (6 clones); was H-2b restricted and recognized only RBL-5 and HFL/b tumor cells of the Friend, Moloney, or Rauscher family (1 clone); showed a total lack of target specificity (21 clones); or lacked detectable cytotoxic activity (2 clones). Thus, the highly heterogeneous constitution of CTL populations generated against MuLV-induced tumors in BALB/c and BALB.B mice was demonstrated. (40 Refs)

48. IMPAIRMENT OF SPLENIC NATURAL KILLER CELL ACTIVITY OF MICE INFECTED WITH THE POLYCYTHEMIC STRAIN OF FRIEND LEUKEMIA VIRUS.

Migliorati G, Jezzi T, Favalli C, Garaci E, Rossi RB, Bonmassar E
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Cancer Immunol Immunother; 12(2):177-179 1982

The effect of polycythemic strain Friend leukemia virus (FLV-P) infection on natural killer (NK) activity in FLV-P-susceptible DBA/2 inbred mouse recipients was examined. Spleen cells were collected from 4-wk-old control or FLV-P-infected donors on days 2, 7, 14, 21, and 28 after virus inoculation. Pools of four spleens each were tested for NK activity at various attacker:target ratios. A significant decrease of NK activity occurred as early as 7 days after infection. From day 14 onward, splenic NK function of infected mice was minimal. Moreover, an actual decrease of NK activity of the whole spleen occurred in these mice, as evidenced by the extremely low levels of lytic units per spleen detectable 3 wk after FLV-P infection. A limited but progressive decline of NK activity was found in the spleen of control non-infected donors, presumably expressing an age-dependent decrease of NK levels in the organ. The mechanism of suppression is discussed. It was suggested that suppression could be based on cell-mediated impairment of NK effector function, or on antigenic competition from splenocytes expressing NK antigens elicited by FLV-P. (19 Refs)

49. MURINE LEUKEMIA. PROPOSED ROLE FOR GANGLIOSIDES IN IMMUNE SUPPRESSION.

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Eur J Cancer Clin Oncol; 18(1):89-98 1982

Glycolipid-bound sialic acid levels were elevated two to four-fold in the sera of two strains of mice bearing thymic lymphoma produced either spontaneously (AKR/J) or due to chemical carcinogenesis [Swiss mice injected with 5-(3,3-dimethyl-l-triazeno)imidazole-4-carboximide]. The serum glycolipid-bound sialic acid level reflected the tumor burden of the AKR/J mice during the early stages of leukemogenesis. Furthermore, the elevation was found to coincide with the ontogenesis of thymic lymphoma and not to be simply an age-dependent phenomenon. TLC analysis of Florisil column-purified gangliosides from the sera of AKR/J and Swiss mice suggested presence of gangliosides with mobilities very close to GM2 and GM3 standards respectively. On the premise that the elevated glycolipid levels in circulation might interfere with normal lymphocyte functions, the immunoinhibitory properties of exogenously added mixed gangliosides were examined on tests of in vitro correlates of the immune response. Gangliosides inhibited concanavalin A and lipopolysaccharide-induced [3H]-thymidine, [14C]-leucine and [5H]-lysine uptake by normal AKR/J mouse thymocytes and spleen cells. Mixed gangliosides also suppressed the two-way mixed lymphocyte reaction of AKR/J x Swiss and AKR/J x DBA/2 spleen cells. These and other results strongly suggest a general immunologically relevant role for gangliosides in the ontogeny of thymic lymphoma of mice. (Author abstract) (39 Refs)

50. INFLUENCE OF SELECTIVE ABSENCE OF H-2KKAPPA ON GROSS VIRUS LEUKAEMIAS IN VITRO AND THE IMPLICATIONS FOR IN VIVO SURVEILLANCE OF LEUKAEMIA.

Festenstein H, Schmidt W, Alonzo A, Leben L
Dept. Immunology, London Hosp. Medical Coll., London, England

Protides Biol Fluid Proc Colloq; 29:231-235 1982

Results are presented of direct complement dependent cytotoxicity tests using anti H-2Kkappa (H-2Kk) monoclonal antibody on five primary AKR leukemias. These and earlier results permit the conclusion that the absence/reduction of the H-Kk gene product is not uncommon in Gross virus leukemia. In search of the biological implication of this finding, a comparison was made of the ability of the K-GV BALB/c Gross virus tumor, which lacks Kk, and other Gross virus tumors with normal H-2Kk representation, to act as targets in cell mediated lympholysis (CML). Results showed that resistance to syngeneic CML is apparently due to the absence of Kk and is thus a failure of associative recognition. Results suggest a new mechanism of escape of T cell surveillance by leukemic cells which involves selective decrease of the H-2Kk antigens, which in this and other studies, have been shown to serve as elements of associative recognition in Gross virus leukemia. (6 Refs)

51. SOURCES AND BIOLOGY OF REGULATORY FACTORS ACTIVE ON MOUSE MYELOID LEUKEMIC CELLS.

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J Cell Physiol; Suppl1:175-183 1982

The cell types producing granulocyte-colony stimulating factor (G-CSF), the half-life of G-CSF in the serum, and the effects of endotoxin in modifying serum G-CSF levels were studied. Mice used were 3-mo-old male and female mice of the strains C57BL and BALB/c. Following a single iv injection of 5 ug endotoxin, the capacity of the serum to induce differentiation colonies of WEHI-3B cells rises rapidly to a peak at 3-6 hr. Groups of C57BL mice were injected iv with 5 ug endotoxin 4x/wk. Good responses were obtained following the first three injections but thereafter successive responses were weaker and after the seventh injection no significant rises in activity were observed. Irradiation (150-1,200 rad) did not prevent the mice from responding to a subsequent injection immediately after irradiation. Groups of BALB/c nu/nu (congenitally athymic) mice were injected with the same agent. Nu/nu mice exhibited a normal response to the injection and exhibited obvious elevations in serum differentiating activity. Effects of cocultivation of WEHI-3B cells with normal cells were studied. Neither normal BALB/c thymus nor peritoneal cells formed colonies in the type of agar medium used. Addition of thymus cells did not induce differentiation in WEHI-3B colonies. Addition of 10(6) BALB/c peritoneal cells caused a marked differentiation of WEHI-3B colonies. Serum differentiating activity half-life varied between 1.5 and 2.3 hr. Groups of BALB/c mice were sc injected with 10(6) WEHI-3B cells. Recipient mice developed sc tumors within 3-4 wk of transplantation. No elevated levels of differentiating activity were observed. (41 Refs)

52. HEMIN-INDEPENDENT CONTROL OF GLOBIN SYNTHESIS IN FRIEND ERYTHROLEUKEMIA CELLS INDUCED TO DIFFERENTIATE.

Stringer EA, Friend C
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Proc Natl Acad Sci USA; 79(6,part1):1839-1843 1982

A hemin-independent translational inhibitor that prevents synthesis of rabbit globin when uninduced Friend leukemia (FL) cell and rabbit reticulocyte lysates are mixed cannot be detected in FL cells induced to differentiate. Mixing of lysates of FL cells induced with hexamethylene bisacetamide or aminonucleoside of puromycin and rabbit reticulocytes does not cause inhibition of rabbit globin synthesis. Induction also results in the cells acquiring sensitivity to the inhibitor from uninduced FL cells. A reduction in total protein synthesis is observed when uninduced and induced FL cells lysates are mixed. Inhibition does not result from competition by an excess of uninduced FL cell mRNA species for the translational machinery because uninduced FL cell lysates retain their inhibitory activity after treatment with micrococcal nuclease. Rabbit globin mRNA recovered from rabbit reticulocyte lysates that have been incubated with lysates of uninduced FL cells can still be translated effectively, indicating that inhibition does not result from modification of other species of mRNA by uninduced FL cell lysates. A switch to hemin-dependent translational control does not follow induction of differentiation. The rate of amino acid incorporation in induced FL cell lysates, like that in uninduced FL cell lysates, is unaffected by omission of exogenous hemin from the system. Its presence is not required to prevent activation of heme-regulated inhibitor. From these data, it is clear that the control of protein synthesis in FL cells, whether or not they are induced, is different from that regulated by hemin in normal erythroid cells. (Author abstract) (32 Refs)

53. STAGE-SPECIFIC TRANSFORMING GENES OF HUMAN AND MOUSE B- AND T-LYMPHOCYTE NEOPLASMS.

Lane MA, Sainten A, Cooper GM
Sidney Farber Cancer Inst., Boston, MA, 02115
Cell; 28(4):873-880 1982

DNAs of 20 B- and T-lymphocyte neoplasms of human and mouse origin induced transformation of NIH/3T3 cells with high efficiencies, indicating that these neoplasms contained activated transforming genes that were detectable by transfection. Analysis of the susceptibility of the transforming activities of lymphocyte-neoplasm DNAs to digestion with restriction endonucleases indicated that the same or closely related transforming genes were activated in independent neoplasms representative of the same stage of normal cell differentiation. However, different transforming genes were activated in neoplasms representative of different stages of normal B- and T-lymphocyte differentiation. These results indicate that specific transforming genes are activated in neoplasms of discrete stages of differentiation within these cell lineages. (Author abstract) (40 Refs)

54. GENETIC CONTROL OF ANTIBODY RESPONSES TO MOLONEY VIRUS IN RATS.

Jones JM, Gunther E, Soderberg FB
Dept. Pathology, Univ. Arkansas for Medical Sciences, Little Rock, AR, 72205
Leuk Res; 6(1):127-129 1982

Antibody responses to Moloney leukemia virus (M-MuLV) of various strains of rats were examined to determine the role of the major histocompatibility complex (RT1) in generating them. All animals were immunized with three injections of 100 ug M-MuLV. F2 animals of BN (n/n: high responder) and LEW (l/l: low responder) crosses did not show differences in response to M-MuLV p30, which were intermediate. LEW-1N animals, which have the BN high response RT1n gene bred onto a LEW background, gave very low antibody responses to p30, p15, and gp70. Antibody responses of BN-Lrl congenic rats, which have the LEW high response gene to phytohemagglutinin bred onto the BN background, gave responses slightly but not significantly lower to p30 and gp70, as compared to BN rats. Even though studies with F2 hybrids suggest that RT1 may have more effect on response to gp70 than to p30, it appears that non-RT1 genes are important for high antibody responses to M-MuLV because the LEW-1N rats with a high responder RT1n of BN haplotype on a LEW background were low responders. (10 Refs)

55. COMPARISON OF THE RECEPTORS FOR IGE OF VARIOUS RAT BASOPHILIC LEUKAEMIA CELL LINES. I. RECEPTORS ISOLATED BY IGE-SEPHAROSE AND IGE AND ANTI-IGE.

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Immunology; 46(1):107-116 1982

Receptors for IgE of rat basophilic leukemia (RBL) cells, maintained in different laboratories were isolated by means of IgE-Sepharose of IgE and anti-IgE, and characterized by SDS-polyacrylamide gel electrophoresis. All cell lines were found to be associated with a receptor molecule (R) which could be isolated either with IgE-Sepharose or IgE and anti-IgE and a second receptor (H) which could only be isolated with the aid of IgE-Sepharose. The relative amounts of these two molecules as isolated from surface iodinated cells, varied from one RBL cell line to the other and their apparent molecular weights were not identical on all cell lines. Since comparisons were made on the same gel using receptors isolated from cells labeled with different isotopes of iodine, differences in molecular weight must be considered as being intrinsic and not due to methodological variations. These results provide an explanation why differences were observed among receptors for IgE as characterized in various laboratories. In spite of the fact that the various RBL cell lines originated from the same chemically-induced tumor they have, over the years, undergone changes which are reflected in the receptors for IgE. (Author abstract) (27 Refs)

EXPERIMENTAL STUDIES INVOLVING CHEMICAL AGENTS AND IRRADIATION

56. CARCINOGENICITY OF PHENACETIN: LONG-TERM FEEDING STUDY IN B6C3F1 MICE.

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Int J Cancer; 29(4):439-444 1982

Groups of 52 B6C3F1 mice of each sex were maintained on a diet containing 1.25 of 0.6% phenacetin for 96 wk and then fed a basal diet for 8 wk. Control groups consisted of 50 mice of each sex and were fed a basal diet for 104 wk. All animals

were killed at the end of the experiment and all organs were examined histopathologically. Mice that died during the experiment were also autopsied and those that survived for more than 57 wk, when the first tumor was observed, were also included in the effective number of mice. Tumors were found in the kidney, liver, lung, skin, hematopoietic system (leukemia or lymphoma) and occasionally in some other organs. The dose-related induction of renal cell tumors in the male mice fed phenacetin was clearly demonstrated in this experiment. Urinary bladder lesions that developed in the mice of either sex fed 1.25% phenacetin were also considered to be due to the tumorigenicity of phenacetin. Tumors of other organs in either the phenacetin-treated or the control group were regarded as strain-related spontaneous tumors of B6C3F1 mice. (Author abstract) (20 Refs)

57. HAEMATOLOGICAL CHANGES IN EXPERIMENTAL TUMOURS.

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Indian J Med Res; 74:896-903 1981

To study the effects of transplantable, induced and spontaneous tumors on the hematopoietic system of the host, strain A mice were inoculated ip with 1 x 10(7) Sarcoma 180 and Ehrlich's ascites carcinoma cells, Swiss mice with DBA lymphoma cells with similar inoculation size and DBA/2 mice with 1 x 10(5) L1210 leukemic cells. Tumors were induced in Strain A male mice by subcutaneous injection of 0.3 ml 0.133% 3,4-benzo(a)pyrene in olive oil suspension, and spontaneous mammary tumors were obtained from female C3H mice. Generally, normochromic and normocytic anemia was observed in all the cases at the later phases of tumor progression, although mild to moderate anisocytosis in sarcoma 180, DBA lymphoma, Ehrlich's ascites carcinoma and carcinogen-induced tumor were noticed, and poikilocytosis was significant in L1210 tumor-bearing mice. The lymphoid-myeloid ratio was reversed to 1:4 and a progressive neutrophilia with moderate shift to the left occurred with increasing body burden of tumor cells in all the tumor strains. Marked leukocytosis was a rule and a broad spectrum combinations of antibiotics failed to suppress high leukocyte count. Thrombocytosis with heterogeneous population of platelets was evident in all the cases, though in Sarcoma-180, Ehrlich's ascites carcinoma and DBA lymphoma-bearing mice the clotting and bleeding time were prolonged. (Author abstract) (23 Refs)

58. 5-FLUOROURACIL, 1,3-BIS(2-CHLOROETHYL)-1-NITROSOUREA, AND 1-(2-CHLOROETHYL)-3-(4-METHYLCYCLOHEXYL)-1-NITROSOUREA: EFFECT ON THE HUMAN GRANULOPOIETIC SYSTEM.

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JNCI; 68(4):541-547 1982

The reaction pattern of the normal (nonleukemic) human granulopoietic system to single-agent treatment with 5-fluorouracil (FUra) and to a combination of FUra with two nitrosoureas, 1,3-bis(2-chloroethyl)-1-nitrosourea (BCNU) and 1-(2-chloroethyl)-3-(4-methylcyclohexyl)-1-nitrosourea (MeCCNU), was studied serially by morphologic and in vitro culture methods. The granulopoietic toxicity of FUra was acute and rapidly (by day 21) reversible. In contrast, the toxicity of the combination regimens was long lasting. Evidence exists that an early toxicity (that of FUra) and a delayed toxicity (that of the nitrosourea) were overlapping. Toxicity of BCNU and MeCCNU was most pronounced at the level of in vitro colony-forming units of the granulopoietic system (G-CFUc). G-CFUc compartments of bone marrow and peripheral blood continued to be reduced in size at the time of recovery of the peripheral blood granulocyte count from nitrosourea-induced toxicity. This finding may be responsible for the cumulative toxicity to the human hematopoietic system that frequently has been observed after repeated administration of nitrosourea compounds. (Author abstract) (46 Refs)

59. INDUCTION OF DIFFERENTIATION IN HUMAN PROMYELOCYTIC LEUKEMIA CELLS BY TUMOR PROMOTERS.

Nakayasu M, Terada M, Adolf W, Opferkuch HJ, Schmidt R, Hecker E, Sugimura T
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J Cancer Res Clin Oncol; 103(1):17-29 1982

The prototype polyfunctional diterpene ester tumor promoter of two-step carcinogenesis in mouse skin, 12-O-tetradecanoylphorbol-13-acetate (TPA), induced differentiation of human promyelocytic leukemia cells (HL-60) in culture. Differentiation of HL-60 cells was characterized by increased phagocytosis, increased lysozyme activity (EC 3.2.1.17) in the growth medium, and changes in morphology to those characteristics of more mature cells resembling macrophages. Many of the cells treated with TPA became aggregated, attaching firmly to culture flasks. The av intracellular myeloperoxidase activity (EC 1.11.1.7) per cell decreased during induction of differentiation by TPA. It was also found that TPA enhanced, rather than inhibited, differentiation of HL-60 cells induced by DMSO. In addition to TPA, several polyfunctional diterpene esters of the tigliane, ingenane, and daphnane type have been tested for their ability to induce morphological and functional changes of HL-60 cells. The activities of the compounds to induce these changes correlated well with their activities as tumor promoters in two-step carcinogenesis in mouse skin. In particular, half the concentrations required for induction of adhesion of the cells to flasks were roughly correlated to the potency of these compounds as tumor promoters. Among the compounds tested, phorbol-12,13-didecanoate (PDD), ingenol-3-hexadecanoate, Pimelea factor P1 and Pimelea factor P2 were as active as TPA, while methyl-TPA and 4alpha-PDD were much less active. Phorbol and ingenol were totally inactive up to a concentration 10,000-fold higher than that of TPA. (Author abstract) (28 Refs)

60. INHIBITORS OF PROTEIN GLYCOSYLATION INHIBIT THE DIFFERENTIATION OF FRIEND ERYTHROLEUKEMIA CELLS.

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Biochim Biophys Acta; 696(3):285-289 1982

Tunicamycin, 2-deoxy-D-glucose and 2-deoxy-2-fluro-D-glucose inhibit dimethyl sulfoxide-induced differentiation of Friend cells. This inhibition, characterized by inhibition of hemoglobin synthesis, is accompanied by a specific inhibition of protein glycosylation. The results of cloning experiments indicate that this inhibition specifically affects cells in the period preceding their commitment. These results suggest that glycoprotein synthesis is a requirement for Friend erythroleukemia

cells in order to initiate the expression of the terminal differentiation program. (Author abstract) (13 Refs)

61. PRELIMINARY EXPERIMENTAL CONTRIBUTION TO THE STUDY OF POSSIBLE CARCINOGENIC ACTIVITY OF TWO HERBICIDES CONTAINING ATRAZINE-SIMAZINE AND TRIFURALIN AS ACTIVE PRINCIPLES.

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Pathologica; 73(1027):707-721 1981

The carcinogenicity and mutagenicity of the herbicides Fogard S and Treflan were studied in vivo in female Swiss albino mice and in vitro in human lymphocyte cultures. The active principles in Fogard S are atrazine (25%) and simazine (37.5%). The active principle in Treflan is trifluralin (44.5%). Groups of 25 mice each received 0.25 ml of 2 ppm Fogard S or Treflan ip or sc, 13x at 3-day intervals. One animal from each group was killed every 15 days up to 7 mo. Necropsies were performed when possible on all animals. One mouse from the sc-Fogard S group, five from the ip Fogard S group, and four from the ip Treflan group were lost to cannibalism and could not be examined. Malignant lymphomas (ML) were found in three mice and mesothelioma (MT) in one mouse from the sc Fogard S group. ML was found in two mice from the ip Fogard S group. ML was found in five mice and MT in one from the sc Treflan group. ML was found in three mice and MT in three mice from the ip Treflan group. Cultures of human lymphocytes were stimulated with phytohemagglutinin and then exposed to 0.2, 0.1, or 0.05 cc of 2 ppm Treflan or 0.2, 0.05, or 0.01 cc of 2 ppm Fogard S. Fogard S did not produce abnormalities in morphology or chromosomal variations. At the higher dose, Fogard S produced a slight decrease in mitoses. Treflan produced significant decreases in the number of mitoses with increasing dose. Chromosomal abnormalities were produced in increased frequencies at the lowest dose. Results indicate a correlation between in vivo administration of either herbicide and tumor formation, as well as a correlation between in vitro Treflan administration and genetic abnormalities. (23 Refs)

62. PHENOXY ACID HERBICIDES CAUSE PEROXISOME PROLIFERATION IN CHINESE HAMSTERS.

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Scand J Work Environ Health; 8(1):70-73 1982

Chinese hamsters 12-20 weeks old were given by gavage saline dilutions of commercial herbicides containing either 2,4-dichlorophenoxyacetic acid (2,4-D) or 4-chloro-2-methylphenoxyacetic acid (MCPA). No other active ingredient was present. Nine daily doses were given at 100 mg/kg. The positive control group received clofibrate (CF: 100 mg/kg/day sc, x 7). All test and control animals were sacrificed 1 day after the last dose. Peroxisomes were chemically localized in liver samples and the areas examined by electron micrographic projection. MCPA and CF significantly increased the size of the peroxisomes (p less than 0.001). CF and 2,4-D also increased significantly the number of peroxisomes (p less than 0.001). CF is chemically related to the two herbicides and has been suggested to exert its carcinogenic action through excess production and/or breakdown of hydrogen peroxide resulting in DNA damage. It is suggested that the increased incidence of soft tissue sarcoma and malignant lymphoma related to exposure to phenoxy acid herbicides may derive from the same mechanism, since both herbicides tested increase the size of or proliferate peroxisomes. (11 Refs)

63. LEUKAEMOGENIC AND MUTAGENIC ACTIVITY OF THE BUTYROPHENON, 4-[4-(4-CHLOROPHENYL)-4-HYDROXY-1-PIPERIDINYL]-1-(4 FLUOROPHENYL)-1-BUTANONE (HALOPERIDOL).

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Carcinogenesis; 3(2):223-224 1982

Development of mainly monocytic-myeloid leukemias was observed in two strains of mice upon ip administration of 4-[4-(4-chlorophenyl)-4-hydroxy-1-piperidinyl]-1-(4 fluorophenyl)-1-butanone (haloperidol), an antipsychotic drug. Haloperidol was also shown to be mutagenic in the Ames Salmonella test system. (Author abstract) (7 Refs)

EXPERIMENTAL STUDIES: DNA TUMOR VIRUSES

64. ISOLATION AND PARTIAL CHARACTERIZATION OF A NUCLEAR ANTIGEN (68/6.3) FROM THE NAMALWA CELL LINE (A BURKITT LYMPHOMA).

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J Cancer Res Clin Oncol; 103(1):7-16 1982

A nuclear antigen was purified from the 0.01 M Tris-HCl/pH 8 extract of nuclei of the Burkitt tumor Namalwa cell line to electrophoretic homogeneity by DEAE cellulose chromatography, affinity chromatography, and preparative isoelectric focusing. The yield of antigens was 0.02% of the nuclear 0.01 M Tris-HCl/pH 8 extract. On two-dimensional gel electrophoresis, the major antigen separated into two adjacent protein spots with mol wt of 68,000 and an approx pI of 6.3 (68/6.3 A and 68/6.3 B). A minor antigen had a mol wt of 61,000 and pI of 6.0 (61/6.0). Fourteen 125I-labeled peptides were obtained from the tryptic digest of the major antigen (68/6.3 A and 68/6.3 B). The amino-acid composition analysis of the purified antigens indicated that the amino acids in the highest content were glycine (15%), glutamic acid (11.6%), and serine (9%); the ratio of acidic to basic amino acids were 1.95. In studies on nucleolytic activity, the purified antigen produced a single-stranded and then a double-stranded cleavage of PM 2 and pBR 322 DNA. This antigen is the first purified nuclear antigen that reacts with the HeLa-specific nucleolar antibodies. (Author abstract) (28 Refs)

65. A MONOCLONAL ANTIBODY DEFINING A BURKITT LYMPHOMA ASSOCIATED ANTIGEN.

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Protides Biol Fluid Proc Colloq; 29:899-902 1982

Reactivity of monoclonal antibody 38-13, obtained by fusing murine myeloma cells with Lewis rat splenocytes sensitized with Daudi cells (human Burkitt lymphoma), was investigated.

Negative results were obtained in all patients with B chronic lymphoid leukemia, acute lymphoid leukemia (T and nonT-nonB), acute myeloid leukemia, acute monoblastic leukemia, Hodgkin's disease, T cell lymphosarcoma, and B cell lymphosarcoma (nodular and diffuse). Positive results were observed in 4/8 patients with B cell Burkitt lymphoma. When the specific reactivity of 38.13 ascites was tested with a panel of cell lines of various origins, both by complement dependent lymphocytotoxicity tests and indirect membrane immunofluorescence assays, all the positive target cells were of Burkitt's lymphoma origin. Negative results were obtained with 15 Epstein-Barr virus positive lymphoblastoid cell lines, 4 T cell lines, a chronic myelogenous leukemia cell line, 4 teratoma cell lines, and one each of melanoma and neuroblastoma. The 38.13 monoclonal antibody may be useful for diagnosis and specific immunotherapy of Burkitt lymphomas. (8 Refs)

66. MONOCLONAL ANTIBODY AGAINST EBV-ASSOCIATED TRANSFORMATION ANTIGEN DETECTED IN VITRO AND IN VIVO.

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Protides Biol Fluid Proc Colloq; 29:739-742 1982

Transformation antigens on the surface of in vitro Epstein-Barr virus (EBV)-transformed B lymphocytes were defined by producing specific monoclonal antibodies. A hybridoma (17D6) was cloned and analyzed for its binding properties to a variety of EBV-positive and -negative B cell lines. The antibody reacted strongly with all of the EBV-positive lines and weakly with the EBV-negative lines. Similarly, a panel of EBV-negative cell lines from a variety of sources reacted only weakly with the 17D6 antibody. When a whole panel of EBV-infected cells from sources other than in vitro infection were tested, all the cell lines containing EBV were as positive as in vitro infected cells, including one cell line derived by spontaneous outgrowth from an EBV-positive individual and one from co-cultivation of normal lymphocytes from a seronegative individual with a nasopharyngeal carcinoma. Burkitt's lymphoma tumor cells reacted only weakly with the 17D6 antibody due to their relatively low levels of the antigen. 17D6-positive cells also were detected in the peripheral blood of infectious mononucleosis (IM) patients. 17D6-positive cells could be detected in the peripheral blood of a patient with chronic EBV infection at higher levels than in patients with acute IM. After recovery, no 17D6-positive cells could be detected. Radioimmunoprecipitation studies suggested that the 17D6 antibody recognizes a polypeptide of 40,000 mol wt. The results indicated that the 17D6 antibody recognizes an EBV-associated transformation antigen on the surface of in vitro and in vivo infected cells. (4 Refs)

67. MIGRATION INHIBITION CAUSED BY EBV-SPECIFIC 48K SUBCOMPONENT OF EBNA AND THE ASSOCIATED 53K CELLULAR PROTEIN.

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Dept. Tumor Biology, Karolinska Institutet, S 104 01 Stockholm, Sweden
Int J Cancer; 29(4):413-416 1982

Leukocytes from EBV-seropositive but not seronegative healthy donors responded with significant migration inhibition to the 48K subcomponent of the Epstein-Barr virus determined nuclear antigen (EBNA), known to carry the virally determined antigenic specificity. A concentration of 10 ug/ml was still effective while 5 ug/ml had no detectable effect. EBNA-associated cellular 53K protein had no effect by itself, but it potentiated the effect of 48K, even if the latter was added at the subliminal concentration of 5 ug/ml. The related 53K protein, isolated from EBV-negative human lymphoma cells, was also effective, whereas the corresponding murine-tumor-associated 53K had no potentiating effect. Immunization of mice with an extract of DNA-binding proteins from EBV-carrying Raji cells, known to contain both 48K and 53K, induced a significant macrophage migration inhibition response, to both human 48K and 53K. Murine 53K was ineffective, however. Human but not murine 53K increased the migration inhibitory activity of subliminal concentrations of 48K in the murine macrophage system as well. These findings suggest that human but not murine 53K may reconstitute with 48K (EBNA) to form a highly immunogenic complex. (Author abstract) (24 Refs)

68. EPSTEIN-BARR-VIRUS-SPECIFIC T-CELL MEMORY IN RENAL-ALLOGRAFT RECIPIENTS UNDER LONG-TERM IMMUNOSUPPRESSION.

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Lancet; 1(8278):923-925 1982

The level of long-term responsiveness of cytotoxic T cells to Epstein-Barr (EB) virus has been measured in peripheral-blood mononuclear-cell cultures from symptom-free renal-allograft recipients under conventional immunosuppression. Eight of 22 patients showed a profoundly impaired responsiveness when compared with healthy control donors. The allograft recipients as a group showed raised antibody titers to EB-virus capsid and early antigens, but within the group there was no clear relation between these antibody titers and the level of EB-virus-specific cytotoxic-T-cell function. These findings are particularly relevant to the pathogenesis of the malignant lymphomas to which renal-allograft recipients are unusually susceptible, in view of the evidence implicating EB virus. (Author abstract) (28 Refs)

69. CELLULAR AND EPSTEIN-BARR VIRUS SPECIFIC DNA POLYMERASES IN VIRUS-PRODUCING BURKITT'S LYMPHOMA CELL LINES.

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Nucleic Acids Res; 10(7):2453-2465 1982

We have determined the levels of cellular DNA polymerases and Epstein-Barr virus specific DNA polymerase in three Burkitt's lymphoma cell lines producing varying amounts of EBV, one of which was induced by 12-O-tetradecanoylphorbol-13-acetate (TPA). There was a proportional increase in the level of EBV-DNA polymerase with an increase in the percent of virus-producing cells. However, there was a reciprocal relationship between the levels of EBV-DNA polymerase and DNA polymerase alpha ie, in cell line containing the highest level of EBV-DNA polymerase, activity of DNA polymerase alpha, but not of DNA polymerase beta, was reduced to an insignificantly low level. TPA does not have any direct effect on activities of either EBV-DNA polymerase or DNA polymerase alpha. EBV-DNA polymerases isolated from cells grown with or without TPA are indistinguishable in their properties such as elution position on phosphocellulose column, molecular weight, mono and divalent cation requirements, pH optimum, and other requirements for optimum activity. Addition of

crude extracts of cells grown in presence of TPA to the purified DNA polymerase alpha did not inhibit its activity indicating that the observed loss was not due to any specific inhibitor present in TPA treated cells. Raji, a non-producer cell line, did not contain EBV-DNA polymerase. There was no induction of EBV-DNA polymerase when Raji cells were grown in presence of TPA. The phenomenon of reduction in the levels of DNA polymerase alpha in cells induced to produce EBV may represent a mechanism by which the host DNA replication is shut off following virus infection. (Author abstract) (36 Refs)

EXPERIMENTAL STUDIES: RNA TUMOR VIRUSES

70. TRANSFORMING GENES OF CHICKEN BURSAL LYMPHOMAS.

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J Cell Physiol; Suppl1:209-212 1982

Transforming genes (TG) in chicken bursal lymphomas (BL), isolation of such TG by molecular cloning, and the specificity of TG activated in neoplasms of different types of differentiated cells are discussed. BL are induced in chickens by infection with lymphoid leukosis viruses (LLV). Transfection assays of DNA of LLV-induced BL indicated that these neoplasms contained TG that induced transformation of NIH 3T3 mouse cells with efficiencies of approx 0.1 transformants/ug DNA. No viral sequences were detected in NIH cells transformed by LLV-induced lymphoma DNA using probes either representative of the entire LLV genome or specific for the LLV long terinmal redundancy, which contains the viral transcriptional promoter. TG of BL detected by transfection were linked to viral DNA, indicating that lymphomagenesis by LLV involved indirect activation of cellular TG at some stage of the disease process. DNA of NIH cell transformed by BL cell line RP-9 DNA was subjected to partial digestion with four-base recognition restriction endonuclease Mbo I and cloned in lambda Charon 30 to produce a library of approx 200,000 phage. Restriction fragments of normal chicken DNA were detected in blot hybridization with lambda ChBlym-1 probe indicating that the lambda ChBlym-1 TG is homologous to normal chicken sequences. Analysis of TG of B and T cells neoplasms of mouse and human origin further indicates that specific TG are activated in neoplasms representative of specific stages of lymphocyte differentiation. Results thus indicate that specific TG are activated in neoplasms of particular differentiated cell types and suggests the hypothesis that neoplasia may result from abnormal expression of genes that are normally involved in differentiation-specific growth control. (15 Refs)

71. GENOME OF RETICULOENDOTHELIOSIS VIRUS: CHARACTERIZATION BY USE OF CLONED PROVIRAL DNA.

Rice NR, Hiebsch RR, Gonda MA, Bose HR, Gilden RV
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J Virol; 42(1):237-252 1982

Reticuloendotheliosis virus is an avian Type C retrovirus that is capable of transforming fibroblasts and hematopoietic cells both in vivo and in vitro. Studies have shown that it consists of a replication-competent helper virus (designated REV) that is responsible for transformation. We used restriction endonuclease mapping and heteroduplex analysis to characterize the proviral DNAs of REV-A and REV. Both producer and nonproducer transformed chicken spleen cells were used as sources of REV proviral DNA; this genome was mapped in detail, and fragments of it were cloned in lambdagtWES-lambdaB. The restriction maps and heteroduplexes of the REV and REV-A genomes showed that (i) REV contains a large fraction of the REV-A gag gene; (ii) most or all of REV-A pol is deleted in REV; (iii) REV contains a 1.1 kilobase segment derived from the 3' end of REV-A pol or the 5' end of env or both; (iv) this env region in REV is followed by a 1.9-kilobase segment which is unrelated to REV-A; and (v) the helper-unrelated segment of REV extends essentially all of the way to the beginning of the 3' long terminal repeat. Therefore, REV appears to be an env gene recombinant. We also found that the REV-specific segment is derived from avian DNA. Therefore, like the other acute transforming viruses, REV appears to be the product of recombination between a replication-component virus and host DNA. Two other defective genomes in virus-producing chicken cells were also cloned and characterized. One was very similar to REV in its presumptive gag and env segments, but instead of a host-derived insertion it contained additional env sequences. The second was similar to the first in its gag and env regions and appeared to contain an additional 1-kilobase inversion of REV-A sequences. (46 Refs)

72. ERYTHROBLAST CELL LINES TRANSFORMED BY A TEMPERATURE-SENSITIVE MUTANT OF AVIAN ERYTHROBLASTOSIS VIRUS: A MODEL SYSTEM TO STUDY ERYTHROID DIFFERENTIATION IN VITRO.

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J Cell Physiol; Suppl1:195-207 1982

The establishment and characterization of a continuous erythroblast cell line (HD3) that retained its capacity to differentiate in response to a temperature shift in an erythropoietin-like factor dependent fashion and the characterization of variant HD3 sublines are described. A continuous cell line (LSCC HD3) was obtained from a culture of ts34-avian erythroblastosis virus (AEV) clone A6 nonproducer cells that had been in crisis for more than 4 mo. LSCC HD3 has been kept in continuous culture for more than 2 yr. The line does not synthesize helper virus-related proteins, but synthesizes large amounts of p75 AEV, the putative transforming protein of AEV. In four HD3 sublines, 75-85% of the cells became strongly benzidine positive after shift to 42 C. The amount of hemoglobin synthesized by these sublines corresponded to those obtained from ts34-AEV-erythroblast strains analyzed in parallel. Results showed that it is possible to isolate HD3 sublines that resemble freshly transformed ts34-AEV-erythroblast strains in their potential to differentiate. Four cell types (erythrocytes, late and early reticulocytes, and erythroblasts) could be distinguished after induction of terminal differentiation in HD3 sublines. A significant proportion of the cells from sublines 2, 32, 40, and 41 differentiated into more mature forms, including erythrocyte-like cells. Results indicated that the same HD3 variant sublines that were unable to produce hemoglobin upon temperature shift in growth medium plus 10(-5) M hemin were also refractory to temperature-induced terminal differentiation. In all sublines inducible with butyric acid, the amounts of hemoglobin detected with the assay which measures hemoglobin of adult and primitive erythrocytes were much larger than those detected with the assay which predominantly detects adult hemoglobins. (32 Refs)

73. LEVELS OF COLONY-STIMULATING AND INHIBITING ACTIVITIES IN CHICKS WITH MYELOBLASTIC LEUKEMIA ARE RELATED TO DISEASE PROGRESSION.

Bryant DL, Smith RE, Dodge WH
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Exp Hematol; 10(3):249-255 1982

Chicks with myeloblastic leukemia induced by avian myeloblastosis virus (AMV) exhibited increased levels of plasma granulocyte/monocyte (GM) colony-stimulating activity (CSA). Chromatography of plasma from AMV-infected chicks revealed that this CSA eluted in the first protein peak from a column of Sephadex G-200. A second protein peak from the same column contained an inhibitor of GM colony-formation. The presence of the inhibitor and the increased CSA was studied during the development of myeloblastic leukemia. The disease course was separated into two distinct phases: (1) an early phase characterized by the onset of viremia, the induction of leukemic colony-forming cells (CFC) is the marrow, and moderately increased marrow cellularity, (2) a late phase characterized by marked increases in the early parameters, dramatic increases in the number of myeloblasts and decreases in the number of erythrocytic cells. Induction of the GM-CFC-inhibitor occurred during the initial stages of the first phase. Increased GM-CSA occurred later in this phase. We conclude that induction of the inhibitor and increased CSA were associated with disease progression rather than ancillary characteristics of frank disease. (Author abstract) (17 Refs)

74. HORMONE-DEPENDENT TERMINAL DIFFERENTIATION IN VITRO OF CHICKEN ERYTHROLEUKEMIA CELLS TRANSFORMED BY TS MUTANTS OF AVIAN ERYTHROBLASTOSIS VIRUS.

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Cell; 28(4):907-919 1982

Chicken erythroblast cell strains and a cell line transformed by ts mutants of avian erythroblastosis virus (AEV) terminally differentiate when shifted to the nonpermissive temperature (42 C). The differentiated cells resemble mature erythrocytes with respect to morphology and ultrastructure, expression of differentiation-specific cell-surface antigens, pattern of protein synthesis and hemoglobin content. Terminal differentiation is dependent on conditions favoring the differentiation of normal erythroid progenitor cells, including an erythropoietin-like factor. Colonies of ts AEV cells grown at 42 C in semisolid medium resemble erythrocyte colonies derived from normal erythroid progenitor cells. The colonies obtained were comparable in size or slightly larger than the late erythroid precursor (CFU-E) colonies. These results suggest that AEV-transformed cells are blocked at a stage of differentiation that is more advanced than that of the uninfected target cells. ts AEV cells are irreversibly committed to terminal differentiation within 20 to 30 hr after shift to 42 C. (Author abstract) (42 Refs)

75. SEQUENCE HOMOLOGY BETWEEN POLYADENYLATED MRNAS FROM TRANSPLANTABLE MOUSE TUMOURS OF DIFFERENT ORIGIN, AS COMPARED TO MRNAS FROM NORMAL ADULT OR EMBRYONIC TISSUES.

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Eur J Biochem; 123(2):407-414 1982

Complementary DNA copies (cDNA) were 3H-labeled and cell-free-synthesized on polyadenylated mRNA templates which had been isolated from the cytoplasm of mouse FLS ascites tumor cells. They were hybridized to RNAs from different mouse origins: ascites tumors (FLS, Ehrlich, Krebs 2) passaged in mice, tissue-cultured Friend erythroleukemia cells, adult liver, adult brain and whole embryos, 10-12 days old. Analysis of the cDNA-RNA reassociation kinetics showed that the total molecular complexity of FLS cells poly(A)-rich RNA is equivalent to 11,000-12,000 different sequences of 1,800 residues each, distributed in the three usual classes of high, middle and low abundancies. All or nearly all of these sequences were also found in Ehrlich and Krebs 2 tumor cells with the same frequency distribution as in FLS cells. When comparing the total number and relative abundancies of poly(A)-rich RNA sequences in ascites tumor cells to other mouse cells, we found slight but reproducible differences for Friend erythroleukemia, more pronounced differences for adult liver or whole embryos, and maximal differences for adult brain. Some of the most abundant poly(A)-rich RNA species common to all tumor strains either did not exist or were much less abundant in normal tissues. Furthermore, the abundant poly(A)-rich RNA sequences which are common to ascites tumor cells and fetal tissues were also found with the same frequency distribution in adult liver, where cell proliferation is negligible. This supports the conclusion that most of the frequent poly(A)-rich sequences, which appeared to be tumor-specific, cannot simply represent normal mitosis gene transcripts and might in fact be related to the expression of malignancy, at least in old-established tumor strains of different tissue origins. (Author abstract) (56 Refs)

76. VIRAL EXPRESSION IN TWO MYELOMONOCYTIC CELL LINES OBTAINED FROM LONG-TERM BONE MARROW CULTURE INFECTED WITH THE FRIEND POLYCYTHEMIA-INDUCING VIRUS (FV-P).

Mathieu-Mahul D, Heard JM, Fichelson S, Gisselbrecht S, Sola B, Larsen CJ
(c/o Larsen) Lab. de Pharmacologie Experimentale, (U.107 INSERM-LOI-CNRS), Dept. d'Oncologie Experimentale, Centre Hayem, Hopital Saint-Louis, 2 place du Dr. Fournier, 75475 Paris Cedex 10, France
Virology; 119(1):59-67 1982

Two subclones of monomyelocytic cell lines (317 and G-31), issued from mouse long-term bone marrow cultures infected with Friend polycythemia-inducing virus, were studied for virus release and viral protein expression. The 317 cell line permanently produced biologically active spleen focus-forming virus (SFFV) and expressed the gp52SFFV which has been described as encoded by the SFFV genome. In contrast, the G-31 cell line was devoid of any SFFV expression although it released Friend helper leukemia virus (F-MuLV). Both lines expressed a new gp70-related glycoprotein with an apparent mol wt of 66,000. This gp66 species was metabolically unstable and was not packaged into viral particles nor released in culture medium. It was recognized by an anti-Rauscher gp70 anti-

serum but not by anti-MCF gp70 or anti-p15E antisera. gp66 was not found in erythroblastic Friend tumor cell lines, in fibroblasts infected with virus released by lines 317 and G-31, or in nonmyelomonocytic infected hematopoietic cells. However, it was constantly observed in cell lines with a myelomonocytic origin established in vivo and in vitro. Therefore, gp66 is a F-MuLV gp70-related product specifically linked to the myeloid lineage. (Author abstract) (23 Refs)

77. FRIEND ERYTHROLEUKEMIA VIRUS COMPLEX: ROLE OF VIRAL COMPONENTS IN MODIFYING ERYTHROID DIFFERENTIATION IN MICE.

Fagg B, Ostertag W
Dept. Microbiology, Univ. California, Irvine, CA, 92717
JNCI; 68(3):457-460 1982

The present study was carried out to determine which component of the polycythemic strain of Friend erythroleukemia virus (FV-P) - Friend helper virus [Friend murine leukemia virus (F-MuLV)] or the replication-defective spleen focus-forming virus (SFFV) - is responsible for inducing erythropoietin-independent erythropoiesis and expansion of the erythroid compartment in infected mice. F-MuLV and SFFV were cloned in SC1 cells to give a cell line 643/22N, which released only F-MuLV and SC204, a nonproducer cell line carrying SFFV. On superinfection with specific helper viruses, SC204 yielded further cell lines, which released SFFV in conjunction with (1) Friend, (2) Moloney, or (3) Gross helper viruses. With the use of an in vitro colony formation assay to monitor erythropoiesis in the bone marrow of inbred DBA/2J mice infected with any of the virus preparations containing SFFV plus helper virus, the erythroid precursor cell population was found to become erythropoietin-independent and amplified; adult mice infected with any of the helper viruses alone did not develop any symptoms of Friend disease. Thus the biologic activity of the FV-P complex was unaffected by replacement of the F-MuLV with an unrelated helper virus (Moloney or Gross). These results indicated that the SFFV component of FV-P is responsible for modifying erythroid differentiation in adult mice. (Author abstract) (22 Refs)

78. DIVERSE EFFECTS: AUGMENTATION, INHIBITION, AND NON-EFFICACY OF 12-O-TETRADECANOYLPHORBOL-13-ACETATE (TPA) ON RETROVIRUS GENOME EXPRESSION IN VIVO AND IN VITRO.

Lipp M, Scherer B, Lips G, Brandner G, Hunsmann G
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Carcinogenesis; 3(3):261-265 1982

The action of 12-O-tetradecanoylphorbol-13-acetate (TPA) on several retrovirus-related functions was investigated in four virus-host cell systems. The following effects were recorded: (i) in STU-mice, infected with the Friend virus complex (Friend murine leukemia virus/Friend spleen focus forming virus) and treated with TPA (50 ng/g) for 1 wk prior to infection, the number of spleen foci increased five-fold over the control. (ii) Addition of TPA (0.04 to 40 ng/ml) to virus-producing cell systems resulted in a two-fold increase of extracellular reverse transcriptase activity. The max response was observed in Friend leukemia virus-producing mouse cells at 0.1 to 0.4 ng TPA/ml and in simian sarcoma virus-producing rat cells at 4 ng/ml. (iii) The efficiency of transformation of BalbC 3T3 cells by Moloney murine sarcoma virus, tested in a focus formation assay, was slightly enhanced by TPA. (iv) TPA inhibited the induction of endogenous virus formation in B cell mitogen-stimulated spleen cell cultures from BalbC mice. (Author abstract) (18 Refs)

79. THE RELATIONSHIP BETWEEN DIFFERENTIATION OF FRIEND ERYTHROLEUKEMIA CELLS AND SYNTHESIS OF PLASMA MEMBRANE-BOUND GLYCOPROTEINS.

Bosman GJ, Boer P, Steyn-Parve EP
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Protides Biol Fluid Proc Colloq; 29:67-70 1982

Changes that plasma membrane-bound glycoproteins go through during dimethyl sulfoxide (DMSO)-induced differentiation of Friend virus-transformed murine erythroleukemia cells (FELC) are reported. When FELC were induced with DMSO in the presence of tunicamycin, Hb synthesis was inhibited, seemingly by arresting the cells just before they became irreversibly committed to differentiation. Results suggest that changes in synthesis of plasma membrane-bound glycoproteins may play a role in the differentiation of Friend erythroleukemia cells. (11 Refs)

80. INDUCTION OF ERYTHROID TUMORIGENIC COLONIES BY FRIEND HELPER VIRUS F-MULV ALONE AND ISOLATION OF A NEW CLASS OF FRIEND ERYTHROLEUKEMIC CELLS.

Shibuya T, Mak TW
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J Cell Physiol; Suppl1:185-194 1982

Induction of pathological and cellular changes by cloned Friend murine leukemia virus (F-MuLV) and induction of tumorigenic erythroleukemic cells and Friend virus colony forming units (CFU-FV) by cloned F-MuLV were studied in BALB/c mice. Increased spleen wt could be detected 5-6 wk after injection of the cloned F-MuLV, accompanied by an onset of anemia with hematocrit dropping to 20% or less. The decrease in hematocrit was accompanied by an increase in the mortality rate in the infected mice. No tumorigenic colonies could be detected in spleens of the mice prior to their deaths which occurred in approx 12 wk. At biweekly intervals from 10-14 wk after infection, 0.5 ml of packed RBC from uninfected BALB/c mice were injected iv into the infected mice. The cells from the enlarged spleens were then transplanted into uninfected BALB/c adult mice. Splenomegaly developed in the recipient mice within 3 wk of transplantation. After two such serial transplants, the spleens were cultured for Friend erythroleukemia cell lines (FCL) and were found to contain them. The morphology of F-MuLV induced CFU-FV was more diffuse in appearance than that obtained from FV-P or FV-A infected spleens. The cells resembled erythroblasts when examined with Wright-Giemsa stain. None of the colonies examined released any detectable replication defective spleen focus forming viruses (SFFV) and the colonies were erythroid in nature. F-MuLV alone, without the SFFV component, can induce a malignant phase of the Friend disease in newborn BALB/c or NIH Swiss mice. (31 Refs)

81. EFFECTS OF METALLOPORPHYRINS ON HEMOGLOBIN FORMATION IN MOUSE FRIEND VIRUS-TRANSFORMED ERYTHROLEUKEMIA CELLS. STIMULATION OF HEME BIOSYNTHESIS BY COBALT PROTOPORPHYRIN.

Chang CS, Sassa S
Rockefeller Univ., New York, NY, 10021
J Biol Chem; 257(7):3650-3654 1982

Mouse Friend virus-transformed erythroleukemia cells in culture undergo erythroid differentiation when treated with a variety of compounds including iron protoporphyrin IX, ie hemin. Exogenous hemin is not only incorporated into hemoglobin in these cells but also stimulates heme biosynthesis. In this study, we examined whether metalloporphyrins other than hemin can also induce differentiation, and if so, whether they can also be incorporated into hemoglobin. Among eight metalloporphyrins examined in culture of these cells, ie Co, Mn, Cu, Mg, Ni, Zn, Sn, and Cd protoporphyrin IX, only Co protoporphyrin (10(-4) M) was found to significantly increase the biosynthesis of heme and hemoglobin. In contrast to hemin-mediated induction of erythroid differentiation, Co protoporphyrin was not incorporated into hemoglobin in Friend cells. These data indicate that Co protoporphyrin induces the formation of heme and hemoglobin in Friend cells and that these increases are due to the enhancement of heme biosynthetic activity. (Author abstract) (31 Refs)

82. A HOST GENE CONTROLLING EARLY ANAEMIA OR POLYCYTHAEMIA INDUCED BY FRIEND ERYTHROLEUKAEMIA VIRUS.

Shibuya T, Mak TW
Ontario Cancer Inst., Univ. Toronto, Ontario M4X 1K9, Canada
Nature; 296(5857):577-579 1982

Two isolates of Friend erythroleukemia virus (FLV), FV-A and FV-P (which was derived from FV-A), have varying hematological effects in regard to hematocrit, polycythemia, and the kinetics of erythropoiesis. Further studies are presented which demonstrate that in addition to the viral contributions, host genes play an important part in determining the nature of the disease induced by Fv-A or FV-P. A new host gene which determines the induction of early anemia or polycythemia by FLV is described. (23 Refs)

83. BIOLOGICAL CHARACTERISTICS OF TYPE C VIRUSES ISOLATED FROM DIFFERENT FRIEND ERYTHROLEUKAEMIC CELLS.

Vinton EC, Woytowicz JM, Levy SB
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J Gen Virol; 59(part1):73-81 1982

We have examined the expression of Type C RNA viruses in different Friend erythroleukemic cell types, distinguished on the basis of increasingly malignant characteristics, which arise during the aging of mice inoculated with the polycythemic Friend virus complex. Most early appearing Friend cells (Type I) expressed ecotropic virus, but cells of later malignant types showed decreased and variable expression. In general, the more malignant cells released less ecotropic virus. Xenotropic virus was detected in low numbers from Type I, II, and IV cells. Two viruses were cloned from Type II tumor cells: a xenotropic virus (II clone 1) and an N-tropic ecotropic virus (II clone 2). No pathogenic activity was found when II clone 1 was inoculated into newborn and adult DBA/2J and NIH/Swiss mice observed for up to 20 mo, where II clone 2 caused a rapid anemic erythroleukemia in both N- and B-type newborn mouse strains. It caused a similar form of leukemia in susceptible N-type adult mice, but at a lower frequency and with a longer latency (usually greater than 5 mo). This finding demonstrated a lack of NB restriction in newborn mice. The virus was much less active in DBA/2J mice from which it had been originally cloned; it also appeared to cause lymphoma or to shorten the latency of spontaneous lymphoma in DBA/2J mice. (Author abstract) (38 Refs)

84. CO-EXPRESSION OF MOUSE AND RAT HEMOGLOBINS IN INTERSPECIFIC HYBRIDS OF MOUSE AND RAT ERYTHROLEUKEMIA CELLS.

Greiser-Wilke I, Steinheide G, Jentsch E, Arndt-Jovin D, Kluge N, Eibl HJ, Ostertag W
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Leuk Res; 6(1):9-15 1982

Hybrids from mouse and rat erythroleukemia cell lines were analyzed. Hybridization was done by a modified lysolecithin-lipid emulsion technique between Friend leukemia mouse cells and D5A1 rat erythroleukemia cells. The hybrids were selected in HAT (hypoxanthine, aminopterin, thymidine) medium. Two mo after culture chromosome analysis gave an almost tetraploid number, with no detectable chromosome loss and all markers present. Analysis of globin by carboxymethylcellulose chromatography after induction of erythroid differentiation by dimethylsulfoxide showed globin chains from both species. These findings demonstrate that both subsets of regulatory genetic material for inducible erythroid differentiation were compatible irrespective of the tumor character of the parental cell lines. (33 Refs)

85. MURINE LEUKEMIA VIRUS-MEDIATED TRANSFORMATION OF A MOUSE EPITHELIAL CELL LINE MMC-E.

Rapp UR, Keski-Oja J
Lab. Viral Carcinogenesis, NCI, Building 560, Room 21-77, Frederick, MD, 21701
Cancer Res; 42(6):2407-2411 1982

Mouse embryo epithelial cells, MMC-E, were malignantly transformed in culture with MuLV derived from C3H/MCA 5 cells chemically induced by 5-iododeoxyuridine. The frequency of transformation was significantly enhanced if infection was followed by treatment with 100 ng of 12-O-tetradecanoylphorbol-13-acetate per ml. The virus transformed cells retained their high plating efficiency in soft agar in the absence of 12-O-tetradecanoylphorbol-13-acetate and formed neoplasms in nude mice. (Author abstract) (24 Refs)

86. CHARACTERIZATION OF AN RNA-DIRECTED DNA POLYMERASE FROM MOUSE SPLEEN INFECTED WITH LEUKAEMIA VIRUS ACTIVATED DURING N-METHYL-N-NITROSO UREA-INDUCED LEUKAEMOGENESIS.

Drescher B, Ehm I, Fey F
Central Inst. Molecular Biology, Acad. Sciences of German Democratic Republic, DDR-115 Berlin-Buch, E. Germany
Acta Virol (Praha); 26(1/2):41-49 1982

An RNA-directed DNA polymerase was purified from mouse spleen infected with leukemia virus activated during N-methyl-N-nitroso urea- (MNU-) induced leukemogenesis. The enzyme was isolated from the microsomal fraction and purified

by successive chromatography of Sephadex G-200 and phosphocellulose. Estimation of mol wt from the sedimentation rate of the purified enzyme in a sucrose gradient gave a value of 70.000. The enzyme had a pH optimum of 7.4, a KCl optimum of 50 mmol/l, an Mn++ optimum of 0.2 mmol/l, and a temperature optimum of 25 C, when (rA)n - (dT)10 was used as the template-primer. It preferred (rA)n - (dT)10 as the template-primer and transcribed (rC)n - (dG)12 and (OMeC)n - (dG)12. A comparison of the properties of this DNA polymerase with the enzyme purified from murine Type C retroviruses showed that the MNU-activated virus enzyme was both biochemically and biophysically indistinguishable from murine leukemia virus DNA polymerases. (Author abstract) (18 Refs)

87. DIFFERENTIATION AND VIRUS EXPRESSION IN BALB/MO MICE: ENDOGENOUS MOLONEY LEUKEMIA VIRUS IS NOT ACTIVATED IN HEMATOPOIETIC CELLS.

Fiedler W, Nobis P, Jahner D, Jaenisch R
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Proc Natl Acad Sci USA; 79(6,part1):1874-1878 1982

The endogenous Moloney leukemia virus (M-MuLV) in the BALB/Mo substrain of mice is activated during the 1st wk after birth. Virus replication occurs in cells of the lymphatic system. Lymphoid cells therefore represent the target cells for virus replication and leukemic transformation. To investigate whether virus activation occurs during lymphoid cell differentiation, hematopoietic stem cells carrying the endogenous Mov-1 genome were transplanted to sublethally irradiated BALB/c mice. Effective colonization of the recipients was demonstrated by Southern DNA hybridization. No activation of the endogenous Mov-1 genome occurred during a 4-mo observation period after the transplantation. Thus, the first step in development of disease in BALB/Mo mice involves activation of the Mov-1 locus in a nonhematopoietic cell followed by superinfection of lymphatic cells and subsequent virus replication and virus spread. (Author abstract) (20 Refs)

88. GLYCOPROTEINS OF FRIEND MURINE LEUKEMIA VIRUS: SEPARATION AND NH2-TERMINAL AMINO ACID SEQUENCES OF GP69 AND GP71.

Linder D, Stirm S, Schneider J, Hunsmann G, Smythers G, Oroszlan S
(c/o Oroszlan) Biological Carcinogenesis Program, Frederick Cancer Res. Facility, NCI, Frederick, MD, 21701
J Virol; 42(1):352-355 1982

The NH2-terminal amino acid sequences (initial 23 residues) of Friend murine leukemia virus gp71 and gp69 were determined and found to be different but highly related. Friend murine leukemia virus gp71 differed from Rauscher murine leukemia virus gp70 in only one position. Friend murine leukemia virus gp69 showed approx 41% homology to these glycoproteins but lacked the glycosylation site (sequon) occurring at position 12 in Rauscher murine leukemia virus gp 70. (Author abstract) (17 Refs)

89. ALLELISM AND LINKAGE STUDIES OF MURINE LEUKEMIA VIRUS ACTIVATION GENES IN LOW LEUKEMIC STRAINS OF MICE.

McCubrey J, Risser R
McArdle Lab. for Cancer Res., Univ. Wisconsin, Madison, WI, 53706
J Exp Med; 155(4):1233-1238 1982

Genes Inc-1 and Inb-1 that interact to enhance ecotropic murine leukemia virus induction in low virus strains of mice were previously found in BALB/c and C57BL/6 (B6) strains of mice, respectively. In order to relate these induction genes to known proviruses, their position in the mouse genome was determined. Classical genetic techniques to determine whether A/J, C3H/He, and SEC strains had a locus allelic to Inc-1 of BALB/c demonstrated that the Inc-1 loci in these mice were tightly linked. No recombinants were recovered in the 149 cultures examined, supporting the hypothesis that these genes are at identical locations in these strains. When B6 mice were mated to C57BR, and the F1 were crossed to BALB/c mice, it was shown that B6 and C57BR were allelic for Inb-1. The linkage of Inc-1 with Pgm-1 and Gus-1 was studied: Inc-1 was approx 24 centimorgans (cM) from Pgm-1 and was loosely linked to Gus-1. Inc-1 was on the centromeric side of Pgm-1. Analysis of the linkage of Es-1 to Inb-1 demonstrated that the loci were approx 30 cM apart. These data are consistent with two possible explanations: Inc-1 and Inb-1 are part of the virus-inducing genes Cv-1 and Bv-1, respectively, or Inc-1 and Inb-1 are tightly linked regulatory genes. (14 Refs)

90. CONTINUING GERM LINE INTEGRATION OF AKV PROVIRUSES DURING THE BREEDING OF AKR MICE AND DERIVATIVE RECOMBINANT INBRED STRAINS.

Steffen DL, Taylor BA, Weinberg RA
Worcester Foundation Experimental Biology, Shrewsbury, MA, 01545
J Virol; 42(1):165-175 1982

The gel electrophoresis-hybridization technique of Southern was used to analyze genetically transmitted proviruses coding for the AKV strain of murine leukemia virus. We were able to identify the restriction endonuclease EcoRI fragments containing two previously unidentified, genetically transmitted AKV proviruses of AKR mice. Comparison of different sublines of AKR mice revealed considerable heterogeneity in their complement of germ line proviruses. This heterogeneity provides evidence that the provirus complement of AKR mice is not stable. Rather, the number of genetically transmitted proviruses increases during inbreeding. Examination of a series of sublines of the C3H strain indicated that this amplification is dependent on viremia. We estimate that, in viremic strains of mice, one new provirus becomes fixed in the germ line every 15 to 30 yr. (Author abstract) (20 Refs)

91. FV-1 DETERMINANTS IN XENOTROPIC MURINE LEUKEMIA VIRUSES STUDIED WITH BIOLOGICAL ASSAY SYSTEMS: ISOLATION OF XENOTROPIC VIRUS WITH N-TROPIC FV-1 ACTIVITY IN THE CRYPTIC FORM.

Sakai K, Narita H, Adachi A, Tsuruta S, Yorifuji T, Ishimoto A
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J Virol; 42(1):331-336 1982

By a biological assay system using phenotypically mixed ecotropic and xenotropic murine leukemia viruses, we investigated whether in the virions of a xenotropic virus there is N- or B-tropic Fv-1 determinant in active form. The existence of

N-tropic Fv-1 determinant was demonstrated in SL-XT-1 xenotropic virus isolated from the spleen of a 3-mo-old SL mouse, and the N-tropic Fv-1 tropism was confirmed by analysis of the phenotypically mixed viruses harvested from clonal SC-1 cells doubly infected with the SL-XT-1 and B-tropic ecotropic viruses. However, neither N- nor B-tropic Fv-1 determinant was demonstrated in any xenotropic viruses isolated from embryo cells of BALB/c, NZB, or DBA/2 mice, or Cas E 1-IU, a xenotropic-like virus isolated from a wild mouse. (Author abstract) (19 Refs)

92. LEUKEMOGENESIS BY BOVINE LEUKEMIA VIRUS: PROVIRAL DNA INTEGRATION AND LACK OF RNA EXPRESSION OF VIRAL LONG TERMINAL REPEAT AND 3' PROXIMATE CELLULAR SEQUENCES.

Kettmann R, Deschamps J, Cleuter Y, Couez D, Burny A, Marbaix G
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Proc Natl Acad Sci USA; 79(8,part1):2465-2469 1982

The DNA from 17 lymphoid tumors induced by bovine leukemia virus (BLV) was digested with the restriction endonuclease EcoRI. Filter hybridization analysis using radioactive probes specific for the BLV genome showed that all tumors contained at least one or a portion of one provirus. Digestion of these proviruses with Sac I demonstrated that deletions occurred in about 25% of the cases and involved sequences located in the 5' half of the provirus. No sequence homology was observed between the cloned proximate cellular sequences flanking two different proviruses at their 3' end and the corresponding sequences in 16 other tumor DNAs, thus showing that a wide range of genomic sites could accommodate BLV proviruses. Transcription of viral DNA including long terminal repeated sequences was not detected, strongly suggesting that viral gene expression is not required for maintenance of the tumor state. No expression of 3' proximate cellular sequences was observed, indicating that no proximate downstream promotion took place in the cases examined. (Author abstract) (18 Refs)

93. DETECTION OF BOVINE LEUKAEMIA VIRUS RNA SEQUENCES IN NON-CULTIVATED PERIPHERAL LYMPHOCYTES BY IN SITU HYBRIDIZATION WITH 3H-LABELLED VIRAL CDNA.

Notzel U, Drescher B, Rosenthal S
Central Inst. Molecular Biology, Acad. Sciences of German Democratic Republic, DDR-1115 Berlin-Buch, E. Germany
Acta Virol (Praha); 26(1/2):33-40 1982

Bovine leukemia virus (BVL) in circulating lymphatic cells of the blood is repressed and has to be activated for its expression. After in situ hybridization of BLV-3HcDNA with a specific activity of 3.9 x 10(7) dpm/ug to noncultivated blood cells from five leukotic cattle, in four of these animals from 0.96% to 1.5% lymphocytes were found to contain BLV-specific RNA sequences. Non-hybridized lymphocytes as well as calf thymus cells, used as controls, gave only 0.47% and 0.39% labeled cells, respectively. After short-term cultivation of white blood cells from these leukotic animals the percentage of labeled cells increased. During the short-term cultivation the number of hybridizing cells from one and the same animal and from all animals, when compared with each other, varied to a high extent. The highest values of BLV-RNA sequences-containing cells from all five animals at different cultivation times were within the range of from 2.4 to 16.2%. (Author abstract) (27 Refs)

94. CANDIDATE PRODUCT OF THE FBJ MURINE OSTEOSARCOMA VIRUS ONCOGENE: CHARACTERIZATION OF A 55,000-DALTON PHOSPHOPROTEIN.

Curran T, Teich NM
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J Virol; 42(1):114-122 1982

Sera from rats bearing tumors induced by inoculation of FBJ murine osteogenic sarcoma virus (FBJ-MSV) nonproducer rat cells precipitate two proteins with mol wt of 55,000 (p55) and 39,000 (p39) from FBJ-MSV-transformed cells. These proteins cannot be precipitated from uninfected cells or cells transformed by other strains of murine sarcoma virus, nor can they be precipitated by sera specific for the viral structural proteins. A methionine tryptic peptide mapping analysis showed that p55 and p39 have little or no homology and that they are not related to the helper virus gag and env gene products. p55 could also be detected among the in vitro translation products of 70S RNA from FBJ murine leukemia virus plus FJB-MSV virions but not among those from FBJ murine leukemia virus alone. This suggests that p55 is encoded by the FBJ-MSV genome, whereas p39, which was not detected among the in vitro translation products, may not be virus encoded. Another difference between p55 and p39 is that p55 is phosphorylated, with most of the phosphate on a serine residue(s), whereas p39 is phosphorylated to a much lesser extent, if at all. No protein kinase activity was associated with p55 and p39 immune complexes under standard conditions. Our data suggest that p55 is a strong candidate for the FBJ-MSV oncogene product. (Author abstract) (32 Refs)

REVIEWS AND OTHER RELATED STUDIES

95. MONOCLONAL ANTIBODIES.

Milstein C
Medical Res. Council Lab. Molecular Biology, Cambridge, England
Cancer; 49(10):1953-1957 1982

Basic research on and clinical applications of monoclonal antibodies are discussed. Antibody structure, recognition and effector functions of antibodies, genetic control of antibodies, and advances in the study of antibodies and monoclonal antibodies through the examination of myelomas and related lymphoproliferative disorders are discussed. The monoclonal antibody produced by an isolated clone is a well-defined chemical which can be produced using nonpurified antigens. Production of monoclonal antibodies through fusion of an antibody-producing cell with a myeloma cell and creation of a permanent hybrid culture is described. A model is presented in which the immunogen is a tumor cell and one of the antigenic determinants is tumor specific. Potentially, monoclonal antibodies may be used as biological markers and therapeutic agents. (18 Refs)

96. GENETIC INTERACTIONS BETWEEN TUMOR VIRUSES AND HOST CELLS.

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Cancer; 49(10):1958-1962 1982

Accomplishments in the field of tumor virology over the past 25 yr are reviewed. The list of viruses known to cause

tumors in nature or in laboratory systems has expanded greatly. The oncogenic viruses include retroviruses, herpesviruses, papovaviruses. Dramatic changes have taken place in the study of the genetic interactions between tumor viruses and virus-transformed cells, in searches for virus causation of tumors, and for a genetic and biochemical basis of malignant transformation. Polyoma viruses, adenoviruses, and retroviruses analyzed in mouse or hamster systems are discussed in relation to tumorigenesis. Infectious virus need not be present for tumor induction. Discoveries related to genetic interactions between viral and host cell genes in retrovirus leukemogenesis include the following: viruses produced directly from the inherited endogenous retroviral genes in the mouse are not tumorigenic; during the course of spreading infection, genetic recombinants arise between genomes of the infectious virus and the defective viral genes in the chromosomes of the host; a similar type of recombination can take place between infectious retroviruses and cellular genetic information; in B-lymphocytes transformed by avian retrovirus, only a piece of the virus genome may remain, analogous to the defective genome insertions seen with DNA tumor viruses. Other aspects of tumor virus DNA-host cellular DNA interactions are discussed. (49 Refs)

97. CANCER AS A RESULT OF A FAULTY DIFFERENTIATION?.

Hobom B
No affiliation given
MMW; 124(9):16 1982

Recently reported evidence that supports a possible relationship between malfunction of differentiation mechanisms and development of cancer is summarized. It is noted that myeloblastic leukemia cells of mice produce excessive amounts of a differentiation factor. Researchers have identified 18 genes in Drosophila in which mutations can cause disruptions of normal differentiation processes. The existence of oncogenes is discussed; such genes function normally in cellular regulation processes but, upon mutation, cause disturbances in differentiation and produce cancer cells. (no Refs) (In GER)

98. CANCERS OF CHILDHOOD.

Simone JV, Cassaday JR, Filler RM
St. Jude's Children's Res. Hosp., Memphis, TN
Cancer - Principles and Practice of Oncology. DeVita VT, Hellman S, and Rosenberg SA, ed. Philadelphia, Lippincott, 1926 pp., 1982.

Childhood cancers are reviewed with respect to etiology, clinical features, diagnosis, prognostic factors, and treatment. Chemotherapy, surgery, and radiotherapy of pediatric tumors are discussed. Childhood leukemias, non-Hodgkin's lymphoma (T-cell lymphoblastic lymphoma of the mediastinum, Burkitt lymphoma, non-Hodgkin's lymphoma of the bone), neuroblastoma, Wilms' tumor, rhabdomyosarcoma, Ewing's sarcoma, hepatic tumors, retinoblastoma, germ cell tumors (sacrococcygeal teratoma, germ cell tumors of the testis), and histiocytosis X are discussed. In general, childhood cancers are more responsive to current therapeutic methods than tumors in adults. Remarkable therapeutic success has been achieved in Wilms' tumors, acute lymphocytic leukemia, retinoblastoma, and lymphoma. Studies of childhood leukemias have been useful for testing hypotheses of cancer therapy generated in animal systems. Once an effective therapy has been discovered for an almost universally fatal malignancy, then modifications can be studied to minimize the physical and psychosocial late effects. Because it appears closer to the etiological event in time, childhood cancer has provided an opportunity to study associations and potential etiological factors. Complex schema of etiology have been proposed, sometimes involving two or more events for cancer to develop. (503 Refs)

99. HODGKIN'S DISEASE AND THE NON-HODGKIN'S LYMPHOMAS.

DeVita VT, Hellman S
NCI, Bethesda, MD
Cancer - Principles and Practice of Oncology. DeVita VT, Hellman S, and Rosenberg SA, ed. Philadelphia, Lippincott, 1926 pp., 1982.

Hodgkin's disease (HD) and the non-Hodgkin's lymphomas (NHL) are discussed with respect to etiology and epidemiology, pathology, natural history, disease evolution, diagnosis and staging, clinical staging, immunologic abnormalities, radiation therapy of HD, chemotherapy of NHL, current recommendations for treatment of HD by stage, the place of radiation in the treatment of NHL, combination chemotherapy of NHL, and special considerations in the treatment of patients with advanced diffuse large cell lymphomas. Currently, 70% of patients with HD and 50% with NHL are curable. Of the five different pathologic classifications for malignant lymphoma in use throughout the world, that of Rappaport is the most widely used for clinical-pathologic studies and is described in detail. Clinical and pathological Stage I and IIA HD should be treated with mantle and paraaortic field radiation and, in patients with lymphocyte depleted histology, total nodal irradiation (TNI) and chemotherapy. Stages I and IIA disease with large mediastinal masses may be treated by a variety of methods, including combination chemotherapy (CC) with radiation (R) to areas of bulk disease, R as in other Stage I and IIA patients then salvage chemotherapy or chemotherapy alone. Pathological Stage IIB should be treated with subtotal nodal irradiation, while those with clinical Stage IIB should receive TNI with or without chemotherapy. Combination TNI and CC should be used for patients with pathological stage IIIA. Stage IIIB patients should receive CC with or without R. Stage IVA and IVB patients should receive CC. Nodular Lymphoma Stage I and II should receive localized R. Stages III and IV should be entered on clinical trials. Diffuse lymphoma Stage I and II should received local R; all others should receive CC. (484 Refs)

100. LYMPHOMA AND THE PAROTID GLAND.

Nichols RD, Rebuck JW, Sullivan JC
2799 W. Grand Blvd., Detroit, MI, 48202
Laryngoscope; 92(4):365-369 1982

The rich parotid lymphatic network makes necessary the inclusion of benign and malignant lymphoid disease in the differential diagnosis of parotid swelling. This area is affected directly by lymphoma in many clinical situations and has an indirect relationship with lymphoma through Sjogren's syndrome. These associations can produce uncertainty about the etiology and significance of parotid masses. Patients with Sjogren's have a spectrum of lymphoproliferative disorders from benign lymphoepithelial disease (BLD) to lymphoma and a significantly greater incidence of the latter than the general population. Nine patients with lymphoma and also benign and malignant lymphoid disease in the parotid illustrate various diagnostic considerations. These include that both benign and malignant parotid lymphoid pathology are seen with systemic lymphoma, that lymphoma can co-exist with BLD, may be misdiagnosed as BLD, and can develop in the same gland after appearance of BLD. (Author abstract) (18 Refs)

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CHEMICAL CARCINOGENESIS

1. TOXICITY AND METABOLISM OF ACRYLONITRILE.
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Kimball RF, Munro NB
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Hull LA
104 Depot St., New Sharon, IA, 50207
Med Hypotheses; 8(2):113-133 1982

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Goloborod'ko OP, Veremeenko KN
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EPIDEMIOLOGY AND ETIOLOGY OF HUMAN LYMPHORETICULAR MALIGNANCIES: VIRAL STUDIES

1. A RETROVIRUS ASSOCIATED WITH HUMAN ADULT T CELL LEUKEMIA: IN VITRO ACTIVATION.

Hinuma Y, Gotoh Y, Sagamura K, Nagata K, Goto T, Nakai M, Kamada N, Matsumoto T, Kinoshita K
Inst. Viral Res., Kyoto Univ., Shogoin Kawahara-machi, Sakyo-ku, Kyoto 606, Japan
Gan; 73(2):341-344 1982

Presence of adult T cell leukemia antigen (ATLA) was studied in the mononuclear cell fractions of peripheral blood derived from 11 patients (9 men, 2 women; 48-83 yr old) with adult T cell leukemia (ATL), from a 54-yr-old man with mycosis fungoides (MF), and from 8 healthy adults (6 men, 2

HE 20.3173/2:

women; 21-44 yr old). The mononuclear cell fractions were cultured in the presence and/or absence of interleukin-2 (IL-2) or T cell growth factor. Some of the fractions were also examined with electron microscopy for virus particles. ATLA positive cells were not detected in any of the cell preparations examined prior to culturing. However, ATLA-bearing cells were observed in the cultures from 6/11 ATL patients and 1/2 ATLA antibody-positive healthy subjects. No ATLA-bearing cells were detected in cultures of one patient with MF and six ATLA antibody-negative healthy subjects. High percentages of ATLA positive cells were found 2-3 days after starting cultures without IL-2; the ATLA were located in the cytoplasm of rather small leukemic cells and were often aggregated. The ATLA-bearing cells in cultures supplemented with IL-2 for a greater than 2 wk were large and often multinuclear with blastoid morphology. Presence of Type C virus particles was observed with electron microscopy in ATL-derived cultures with a high percentage of ATLA positive cells. The results showed that (1) peripheral blood cells of many patients with ATL contain sufficient information for ATLA or ATL virus (ATLV) formation in a repressed form, and suggest that (2) ATLA is associated with ATLV and (3) ATLV is present not only in ATL patients but also in anti-ATLA positive healthy individuals. (6 Refs)

2. ASYMPTOMATIC TYPE C VIRUS CARRIERS IN THE FAMILY OF AN ADULT T CELL LEUKEMIA PATIENT.

Miyoshi I, Taguchi H, Fujishita M, Niiya K, Kitagawa T, Ohtsuki Y, Akagi T
Dept. Medicine, Kochi Medical Sch., Oko-cho, Nankoku-shi, Kochi-ken 781-51, Japan
Gan; 73(2):339-340 1982

Serologic and virologic studies were performed in 14 members of the family of a 49-yr-old male patient with adult T cell leukemia (ATL). The patient and family lived in Kochi, an area where the incidence of ATL appears to be relatively high. ATL antigens (ATLA) and Type C virus particles were detected in short-term cultures of peripheral lymphocytes from 4/5 family members who were ATLA antibody positive. The five ATLA antibody positive family members were all asymptomatic and hematologically normal except for one member, in whom a persistent leukocytosis with several percent abnormal lymphocytes had been observed for two yr. It was not yet determined whether vertical or horizontal infection was involved in the virus transmission in this family. (5 Refs)

3. SERO-EPIDEMIOLOGIC STUDIES ASSOCIATE THE HUMAN T-CELL LEUKEMIA-LYMPHOMA VIRUS (HTLV) WITH ADULT MALIGNANCY OF MATURE T-CELLS (MEETING ABSTRACT)

Robert-Guroff M, Kalyanaraman VS, Sliski A, Blattner W, Catovsky D, Sarngadharan MG, Gallo RC
Litton Bionetics, Inc., Kensington, MD, 20895
Fed Proc; 41(3):689 1982

HTLV, a unique human retrovirus (RNA tumor virus), was isolated from cells of patients with lymphomas and leukemias of mature T-cells. Surveys of sera for antibodies to HTLV have shown HTLV to be rarely associated with such diseases in the US, but strongly linked to Japanese adult T-cell leukemia (ATL), lymphosarcoma T-cell leukemia (LCL), and peripheral T-cell lymphoma. LCL is a malignancy of mature T-cells seen in some Caribbeans. ATL is a similar disease clustered geographically in Southwest Japan. Sera of 19 of 22 ATL patients and 3 of 3 LCL patients had antibodies to HTLV p24 and p19 as determined by radioimmunoprecipitation of p24 or by competition radioimmunoassay with a monoclonal anti-p19. Among sera of relatives of sero-positive patients, 20% were also positive, supporting the infectious nature of HTLV. Other normal donors lacked antibodies to HTLV, except for some healthy Japanese in the ATL endemic area, suggesting widespread viral exposure. Sera of children in the US with leukemias, lymphomas, and solid tumors were negative, as were sera from numerous adults with various neoplasias. While HTLV is thus not prevalent in this country, it may play a role in the etiology of mature T-cell neoplasias in other geographic locales. (no Refs)

4. EPSTEIN-BARR VIRUS-INDUCED DISEASES IN MALES WITH THE X-LINKED LYMPHOPROLIFERATIVE SYNDROME (MEETING ABSTRACT)

Purtilo DT, Harada S
Department of Pathology, University of Nebraska Medical Center, Omaha, NE
Lab Invest; 46(1):66A 1982

Analyses of 100 patients with the x-linked lymphoproliferative syndrome (XLP) in 25 kindreds revealed four major interrelated phenotypes: infectious mononucleosis (IM), malignant B cell lymphoma, aplastic anemia, and hypogammaglobulinemia. Eighty-one of the patients have died. Two males were asymptomatic but showed immunodeficiency to Epstein-Barr virus (EBV). Seventy-five patients had the IM phenotype and, concurrently, 17 patients of this group had aplastic anemia. All patients with aplastic anemia died within a week. Aplastic anemia did not accompany hypogammaglobulinemia or malignant lymphoma phenotypes. Hypogammaglobulinemia was detected before IM in three patients, followed IM in five cases, and was not associated with IM in 11 boys. Nine cases of IM appeared to have evolved into malignant lymphoma. However, the majority of patients with malignant lymphoma showed no obvious antecedent IM. One patient had IM following recurrent malignant lymphoma. Twenty-six of 35 lymphomas were in the terminal ileum. Results of immunologic and virologic studies of 15 survivors revealed combined variable immunodeficient responses to EBV-specific antigens. Patients with phenotypes of XLP should be investigated for immunodeficiency to EBV. Persons with inherited or acquired immunodeficiency may be vulnerable to life-threatening EBV-induced diseases. (no Refs)

EPIDEMIOLOGY AND ETIOLOGY OF HUMAN LYMPHORETICULAR MALIGNANCIES: OTHER STUDIES

5. SECOND MALIGNANT NEOPLASMS IN PATIENTS SUCCESSFULLY TREATED FOR HODGKIN'S DISEASE: A CANCER AND LEUKEMIA GROUP B STUDY.

Glicksman AS, Pajak TF, Gottlieb A, Nissen N, Stutzman L, Cooper MR
Dept. Radiation Oncology, Rhode Island Hosp., Providence, RI, 02902
Cancer Treat Rep; 66(4):1035-1044 1982

The recent analyses by the Cancer and Leukemia Group B (CALGB) of patients with advanced Hodgkin's disease entered in CALGB treatment protocols between 1966 and 1974 have substantiated the recognized high susceptibility of these patients to second malignant neoplasm. Protocols 6604, 6712,

6951, and 7251 included radiation therapy and/or chemotherapy with alkylating agents such as mechlorethamine and chlorambucil or nitrosoureas, vinca alkaloids, and procarbazine as induction agents, plus or minus maintenance therapy with vinblastine, or chlorambucil or a repetition of the induction program. The risk of a second malignant neoplasm attributable to each component of curative treatment was analyzed: 798 of 1332 evaluable patients achieved complete remission, with a mean followup of 46 mo. For 27 of these 798 patients, development of a second malignant neoplasm terminated the complete response. Ten patients developed acute myeloid leukemia (AML). For AML, induction chemotherapy with a mechlorethamine-containing regimen, followed by chlorambucil maintenance therapy, had the highest relative risk ratio and life-table estimate. Mechlorethamine without chlorambucil maintenance was not a significant hazard, but chlorambucil without mechlorethamine was associated with a relative risk ratio of 234 and a life-table estimate of 9%. Radiotherapy was not a significant hazard when added to the chemotherapy regimens. For the non-AML second malignant neoplasms, none of the chemotherapy regimens was a greater risk than the others, with a relative risk of 2.8. The addition of radiotherapy significantly increased the incidence of such neoplasms. Patients of all ages had a significant risk of AML but not of the other second malignant neoplasms; however, because of the increasing rate of second malignant neoplasms with the intervening years, the full extent of the risk may not be appreciated for another decade. (13 Refs)

6. ADULT LEUKEMIA RISK AND DIAGNOSTIC X-RAYS: A REANALYSIS OF THE TRI-STATE LEUKEMIA SURVEY DATA.

Ginevan ME, Curtiss JR, Grahn D
Argonne Natl. Lab., Argonne, IL
Adult Leukemia Risk and Diagnostic X-Rays: A Reanalysis of the Tri-State Leukemia Survey Data. Available from National Technical Information Service, Springfield, VA, as NUREG/CR-2234:, 89 pp., 1981.

The present study examined adult leukemia risk as a function of x-ray exposure in a data set consisting of 1,414 leukemia cases and 1,370 controls, using Mantel-Haenszel odds ratio procedures to calculate relative risk for 30 sex/leukemia type/x-ray exposure type categories and between one and six dose levels (measured as number of films). Risk of contracting pneumonia and heart disease for four time periods prior to leukemia diagnosis is also determined. The main finding is that significant excess risk is restricted to two sex/leukemia type/x-ray exposure type categories, males with acute and chronic myeloid leukemia and more than 40 trunk x-rays. Several sex/leukemia type/x-ray exposure types with risks significantly less than 1.0 were also observed. Association of pneumonia and heart disease with leukemia appear to be the result of a reporting bias in that most significant excess incidence of these diseases in leukemics is within 6 mo of leukemia diagnosis. Overall, our results suggest that x-ray related excess leukemia risk is small. (Author abstract)

7. DOSIMETRY AND RISK ESTIMATES IN THE DIAGNOSTIC MEDICAL FIELD (MEETING ABSTRACT)

Land LH
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149th National Meeting of the American Association for the Advancement of Science, January 3-8, 1982, Washington, D.C. American Association for the Advancement of Science 182 pp., 1982.

One of the many risks in medical diagnostic radiation procedures is the risk from the radiation itself. The starting point for estimates of this risk is the determination of the radiation dose either to the whole patient or to a given organ of the patient depending upon the biological end point under study. If the end point is lung cancer, the organ is the lungs; if it is leukemia, the organ is the hematopoietic system; etc. The evaluation of radiation risks has been based on scanty data, many of which are not based on controlled scientific experiments. For example, one important source of medical data is the wartime irradiation of people at Hiroshima and Nagasaki. Although these irradiations occurred in 1945, the retrospective evaluation of dose to individual survivors has periodically undergone redetermination, the latest of which is still under way. In recent years, there has been a concerted effort to improve the accuracy of dose determinations in diagnostic procedures. In many procedures there are several parameters which can be varied, and each can affect the dose to the patient. In mammography the radiation dose to the skin for optimal images can vary by a factor of 20 depending on whether a molybdenum or tungsten target is used in the x-ray tube. A technic for quantifying risk is the development of an appropriate mathematical model. (no Refs)

8. SOCIAL CLASS AND AGE AT DIAGNOSIS OF HODGKIN'S DISEASE: NEW EPIDEMIOLOGIC EVIDENCE FOR THE 'TWO-DISEASE HYPOTHESIS'.

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Cancer Treat Rep; 66(4):689-695 1982

The bimodality in the age-incidence pattern of Hodgkin's disease (HD) suggests that the disease may result from two causal pathways with differing age peaks. Among young adults, HD may develop as a rare consequence of a common infection (probably viral), with risk increasing with age at time of infection. However, among older persons, HD may result from other causes, probably similar to those of the other lymphomas. We evaluated this hypothesis in a population-based, case-control study in eastern Massachusetts involving 326 newly diagnosed cases (patients greater than or equal to 15 years of age) and 650 population controls. These subjects were compared for factors in childhood environment that influence age of exposure to common viruses, including subship size, parental education, and type of housing. Among young adult (15-39 years of age), risk of HD was associated with small family size, single-family housing, and relatively high maternal education, consistent with the delayed infectious exposure hypothesis. Among middle-aged persons (40-54 years of age), a similar pattern of social class risk factors was present. However, among older persons (greater than 55 years of age), risk was not associated with social class; if anything, patients were of somewhat lower social class background than controls. These findings are consistent with the 'two-disease hypothesis,' in that social class risk factors differed between younger and older persons. These findings, coupled with other epidemiologic observations, suggest that the pathogenesis of HD among older persons is independent of that among younger persons. (Author abstract) (10 Refs)

9. PSEUDOLYMPHOMA WITH MYCOSIS FUNGOIDES MANIFESTATIONS, HYPERRESPONSIVENESS TO DIPHENYLHYDANTOIN, AND LYMPHOCYTE DISREGULATION.

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Cancer; 49(11):2305-2314 1982

Three patients receiving diphenylhydantoin (DPH) were seen with a reversible process suggesting mycosis fungoides. Clinical and laboratory manifestations included generalized pruritic exfoliative erythroderma, eosinophilia, lymphadenopathy, hepatosplenomegaly, circulating Sezary cells, epidermal Pautrier's microabscesses on skin biopsy, and moderate liver dysfunction. Studies of the distribution and function of the various lymphocyte subpopulations from these patients showed: (1) an increase in the relative and absolute number of T lymphocytes (85-92%); (2) significant stimulation of lymphocyte-blastic transformation by DPH and low response to pokeweed mitogen stimulation; (3) the impaired ability of Tgamma lymphocytes to suppress B-cell differentiation and immunoglobulin production. With only one exception, 15 symptom-free patients on DPH showed none of these abnormalities. The clinical manifestations and immunologic abnormalities of patients with this pseudo mycosis fungoides syndrome remitted 3-4 wk after DPH administration was discontinued. The proliferation of T lymphocytes and the inhibition of the function of tgamma-suppressor lymphocytes noted in these patients may be significant to the development of other types of pseudolymphoma and to that of true lymphoma. (Author abstract) (24 Refs)

EPIDEMIOLOGY AND ETIOLOGY OF NON-HUMAN LEUKEMIA AND LYMPHOMA

10. EFFECTS OF LIFETIME INGESTION OF 90SR IN BEAGLE DOGS.

Book SA, Spangler WL, Swartz LA

Lab. for Energy-Related Health Res., Univ. California, Davis, CA, 95616

Radiat Res; 90(2):244-251 1982

The effects of lifetime daily ingestion of 1.3, 4, or 12 uCi 90 Strontium (90Sr) were studied in 15 beagle dogs. In utero exposure began with maternal ingestion of 90Sr starting 21 days postconception. Continued 90Sr ingestion resulted in body burdens of 1.2 to 1.7 uCi 90Sr/kg in dogs fed 1.3 uCi/day. Dogs fed 4 uCi/day averaged from 3.8 to 5.1 uCi 90Sr/kg. Dogs fed 12 uCi/day averaged 10.7 to 15.3 uCi/kg body wt. Dogs on the lowest dose lived from 5.3 to 15.8 yr; those at higher dose levels showed decreased life spans. The 50% survivals were estimated to be 12.5, 6.5, and 5.1 yr for the three groups, respectively. Radiation doses to skeletal tissues varied widely within dosage levels. Causes of death included radiation-induced disease as well as diseases not related to radiation exposure. The largest single cause of death among the fifteen dogs was from the myeloproliferative syndrome, which encompasses both neoplastic hematopoietic disease and preleukemic conditions. (18 Refs)

CYTOGENETIC AND MORPHOLOGIC STUDIES

11. A COLLABORATIVE STUDY OF THE RELATIONSHIP OF THE MORPHOLOGICAL TYPE OF ACUTE NONLYMPHOCYTIC LEUKEMIA WITH PATIENT AGE AND KARYOTYPE.

Rowley JD, Alimena G, Garson OM, Hagemeijer A, Mitelman F, Prigogina EL

Box 420, 950 East 59th St., Chicago, IL, 60637

Blood; 59(5):1013-1022 1982

Data on the chromosome analysis of leukemic cells from consecutive patients with nonlymphocytic leukemia from six independent laboratories in the United States, Europe, and Australia were combined. The karyotypic pattern determined with banding was correlated with the patient's age and the morphological type of leukemia according to the FAB classification. Of the 503 patients in the combined study, 260 had acute myeloblastic leukemia (AML, M1 and M2), 142 had acute myelomonocytic leukemia (AMMoL, M4), 43 had acute monocytic leukemia (AMoL, M5), 30 had erythroleukemia (EL, M6), and 28 had acute promyelocytic leukemia (APL, M3). The percentage of patients with an abnormal karyotype was higher in EL (63%) and AML (59%) than in AMMoL (40%) and AMoL (42%). Loss of no. 5 and/or no. 7 occurred in 30% of all EL patients, in 19% of all AML patients, and in only 7% of AMMoL, in 5% of AMol, and in 4% of APL patients. These observations are significant because patients with ANLL secondary to aggressive therapy for a primary malignant disease tend to have AML or EL, and the majority have-5 and/or-7. These same morphological types of leukemia and the same abnormalities,-5 and/or-7, are also increased in patients with ANLL de novo who have a history of occupational exposure to potentially mutagenic substances. In the future, the type of leukemia and the particular karyotypic pattern may be useful in identifying a subset of patients with ANLL de novo whose leukemia may be mutagen-induced. (35 Refs)

12. CYTOGENETIC AND HEMATOLOGIC FINDINGS IN ACUTE MYELOGENOUS LEUKEMIA, M2 ACCORDING TO THE FAB CLASSIFICATION.

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Gan; 73(2):212-216 1982

Chromosome banding studies on leukemic cells from 12 patients with acute myelogenous leukemia (AML), M2 according to the FAB classification, were performed. In eight cases, chromsome abnormalities were observed; among these eight, six were found to exhibit a common chromosome abnormality, ie, t(8;21)(q22;q22). The present findings strongly support the view that AML with t(8;21)(q22;q22) represents a definite subgroup within the general category of AML; this translocation has not been observed in more than 100 cases of leukemias other than AML M2. When the chromosome findings were collated with the hematologic and clinical data, it was found that the cases with t(8;21)(q22;q22) were not distinguishable from those with karyotypes other than the translocation in M2, in terms of hematologic and clinical findings. (Author abstract) (14 Refs)

13. MEANING OF CHROMOSOMAL ABNORMALITY IN LEUKEMIA.

Tomonaga Y, Sadamori N, Matsunaga M, Tagawa M, Ichimaru M
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Nippon Rinsho; 39(8):2773-2779 1981

The findings primarily obtained in the examination of chromosome stained with the bone marrow direct method are described. The highly disease specific chromosomal abnormality, the Philadelphia chromosome (Ph1) is a small marker chromosome, and found in 90% of chronic myelocytic leukemia (CML). Ph1 exists prior to the appearance of clinical symptoms of CML, and the Ph1 clone still remains in remission after therapy; in contrast, the abnormal clone disappears in complete remission of acute leukemia. When CML converts into the acute state, new chromosomal abnormalities in addition to Ph1 appear in 75 - 80% of the cases. Therefore, it can be a criteria for the early diagnosis of acute state conversion. In combining with examination of clinical types of acute state conversion, leukemia cell types, immunological markers, and terminal deoxynucleotidyl transferase activity, Ph1 and additional other chromosomal abnormalities can be used for the estimation of prognosis and selection of therapy. Clones with chromosomal abnormalities can be found in about 50% of acute non-lymphocytic leukemia, but a common marker such as Ph1 in CML is not yet known. However, some close correlation between disease type and chromosomal abnormality is beginning to show up after application of differential chromosome staining method. Two well known such chromosomal abnormalities are 8; 21 translocation and 15; 17 translocation, the former is seen in acute myelocytic leukemia and the latter in acute premyeloblastic leukemia. Other chromosomal abnormalities and their possible association with diseases such as preleukemia, and myeloproliferative syndromes are described. (27 Refs) (In JPN)

14. CHROMOSOMAL ANOMALIES IN LEUKEMIAS.

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Rev Prat; 32(12):857-860 1982

Techniques of study, different types, non-aleatory character, and prognosis of chromosomal anomalies in leukemia are reviewed. Chronic myeloid leukemia is characterized by the Philadelphia chromosome, which is present in 85-95% of cases. In acute nonlymphoblastic leukemia the most common anomalies are trisomy 8, monosomy 7, and either partial or total monosomy 5. In acute lymphoblastic leukemia the Philadelphia chromosome may be present; anomalies of the long arm of chromosome 6 have been noted. In chronic lymphocytic leukemia, determination of the real frequency and specificity of the observed chromosomal anomalies is especially difficult. (14 Refs) (In FRE)

15. IDENTIFICATION OF THE CONSTANT CHROMOSOME REGIONS INVOLVED IN HUMAN HEMATOLOGIC MALIGNANT DISEASE.

Rowley JD
Dept. Medicine, Univ. Chicago, Chicago, IL, 60637
Science; 216(4547):749-751 1982

Specific consistent chromosome translocations are regularly observed in certain human leukemias and lymphomas. For the myeloid leukemias, the constant recombinants are: the long arm of 9 to chromosome 22 in chronic myeloid leukemia, the long arm of 21 to chromosome 8 in acute myeloblastic leukemia, and the long arm of 17 to chromsome 15 in acute promyelocytic leukemia. Three related translocations are seen in Burkitt lymphoma and B cell acute lymphocytic leukemia; in each one, chromosome 8 is involved with chromosome 2, 14, or 22. Analysis of a complex translocation affecting chromosomes 8 and 14 indicates that the translocation of chromosome 8 to chromosome 14 is the critical constant rearrangment. The analysis of the DNA at the translocation sites of these chromsomes, rather than the reciprocal of each translocation, appears to be the most productive focus for initial study. The various immunoglobulin loci are located on chromosomes 2, 14, and 22, the chromosomes regularly involved in translocations in Burkitt lymphoma and B cell acute lymphocytic leukemia. (Author abstract) (30 Refs)

16. CHROMOSOMES, CANCER, AND RADIOSENSITIVITY (MEETING ABSTRACT)

Samouhos E
Radiation Therapy Service, Veterans Administration Medical Center, Martinez, CA, 94553
Am J Clin Oncol; 5(2):136 1982

Some specific chromosomal abnormalities are associated with certain cancers. The earliest description of such a specific association is that of the Philadelphia chromosome and myelogenous leukemia (1960). Other congenital karyotype abnormalities are associated with specific cancers. Examples are Down's syndrome with leukemia and Klinefelter's syndrome with male breast cancer. Genetic diseases of increased chromosome breakage, or of defective chromosome repair, are associated with greatly increased cancer incidence. Three such diseases have been recognized: 1) Fanconi's anemia, associated with leukemias and lymphomas; 2) Bloom's syndrome, associated with acute leukemias and lymphosarcoma; and 3) ataxia telangiectasia, associated with Hodgkin's disease, leukemia, and lymphosarcomas. Ten percent of individuals with ataxia telangiectasia will develop one of these neoplasms. Individuals with certain of these syndromes display an unusually high radiosensitivity. Radiation therapy for cancer has been fatal in patients who received as little as 3000 rad. This remarkable radiosensitivity has been quantitated in cell cultures from such cases. Evidence suggests that the apparent sensitivity may reflect subnormal ability to repair radiation damage. (no Refs)

17. INCIDENCE OF BALANCED 9Q;22Q TRANSLOCATIONS IN THE PATIENTS WITH CHRONIC MYELOGENOUS LEUKEMIA (CML) (MEETING ABSTRACT)

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Am J Hum Gen; 33(6):62A 1982

The saga of improved banding techniques is particularly interesting in relation to the Philadelphia (Ph') chromosome (22q-) whose association with chronic myelogenous leukemia (CML) was discovered by Nowell and Hungerford. This abnormal chromosome, while thought to be a deletion of the long arm of chromosome 22 has now been confirmed as a balanced translocation involving the long arm of chromosomes 9 and 22. Cytogenetic identification is usually performed either by QFQ or by GTG technique. However, by both techniques, the terminal bands of the long arm of chromosome 9 (band q34) and 22(bandq13) are stained negatively. Consequently, the exact nature of this most common translocation may go undetected. We report 52 cases who had been diagnosed as Ph'

positive CML by RFA technique in order to study the precise origin of the Ph' chromosome. We used RFA technique, because terminal bands are positively stained and any minor deletion can easily be detected. Ninety percent cases had 9q;22q translocation, 4% had unusual and 6% cases were without any translocation. The breakpoints were variable on the long arm of chromosome 22 and four types of Ph' chromosomes were recognized. The incidence of very large, large, average and small were 1.92%, 3.85%, 80.77% and 13.46% respectively. (no Refs)

18. CHROMOSOMAL CLONAL EVOLUTION AND BLASTIC CRISIS IN CHRONIC MYELOID LEUKEMIAS (MEETING ABSTRACT)

Bell S, Lozzio CB, Krauss S

University of Tennessee, Birth Defects Evaluation Center, Knoxville, TN

Am J Hum Gen; 33(6):98A 1981

Results of serial chromosome analyses with Giemsa banding techniques are reported for three patients with chronic myeloid leukemia (CML). Chromosomal clonal evolution was found prior and during blastic crisis. The first case was a 32 year old man with a positive Philadelphia chromosome in 50% of the cells cultured from bone marrow at the time the diagnosis was made. A year later 90% of the cells had a Ph1 chromosome plus a translocation t(2;20) (p21;q23) and trisomy 17. This patient died in blastic crisis five months later. The second case was a CML diagnosed at 10 years of age when the bone marrow cultures showed a positive Philadelphia chromosome (Ph1) with translocation t(9;22) (q32;q12) in 100% of the cells. At age 15 he was in relapse and all the cells from bone marrow had a complex translocation of the distal long arm of chromosome 9 including the segment of chromosome 22 rearranged to chromosome 10 at q26. The third case was a Ph1 negative CML diagnosed at age 59 by bone marrow biopsy. An interstitial deletion of chromosome 13-del(13) (q12;q14) was seen in all the cells. Two months later a clone with a translocation t(1;11) (q21;q14) was observed in addition to the deletion 13. After three more months she was in acute crisis. All the cells had the deletion 13, the translocation 1;11 and a translocation involving chromosome 19. After treatment she reached complete clinical remission although 30% of the cells had the three chromosome rearrangements. After consolidation chemotherapy, complete karyotypic remission was reached with all the cells showing a normal karyotype. Correlations between clinical and chromosomal evolution are of special interest. (no Refs)

19. TETRASOMY 21 IN AN INFANT WITH DOWN'S SYNDROME AND CONGENITAL LEUKEMIA.

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Dept. Pediatrics, CMSC 1004, Johns Hopkins Hosp., Baltimore, MD, 21205

Am J Med Genet; 12(1):91-95 1982

A case of tetrasomy 21 is described in a white infant born at 32 wk with Down's syndrome and congenital monocytic leukemia. Fifty cells from a peripheral blood sample obtained at 3 days of age using standard culturing techniques, including phytohemagglutinin stimulation, were studied by quinacrine fluorescent and reverse banding techniques. All cells had 48 chromosomes with four number 21 chromosomes. (29 Refs)

20. CYTOGENETIC FINDINGS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKAEMIA (MEETING ABSTRACT)

Szollar J, Fekete G, Schuler D

2nd Department of Paediatrics, Semmelweis University Medical School, Budapest, Hungary

VI Meeting of the European Association for Cancer Research, October 12-15, 1981, Budapest, Hungary. The European Association for Cancer Research 275 pp., 1981.

Sister chromatid exchange (SCE) studies were conducted in 52 children with leukemia or other malignant condition, and the values compared to those of 40 controls. Children in remission had normal SCE values, whereas those receiving 'intensive' cytostatic therapy showed elevated levels. SCE values were primarily related to the time and dose of preceeding cytostatic drug therapy, but the elevated, or decreased SCE frequencies could characterize the function of lymphocytes too. The uptake of BrdU (5-bromodeoxyuridine) or the 'response to BrdU' seemed to be useful in the follow-up of the malignant disease. Chromosome studies carried out using conventional and banding techniques indicate that the cytogenetic effect, caused by the cytostatic treatment, disappears following the cessation of therapy. Only the cell cycle of 'remission lymphocyte populations' differs from the values of healthy controls. (no Refs)

21. CYTOGENETIC STUDIES OF X-LINKED LYMPHOPROLIFERATIVE SYNDROME (XLP) (MEETING ABSTRACT)

Barnabei VM, Sakamoto K, Seeley JK, Purtilo DT

University of Massachusetts Medical Center, Worcester, MA

Am J Hum Gen; 33(6):98A 1981

The frequencies of chromosomal aberrations and sister chromatid exchanges were measured in lymphoblastoid cell lines and PHA- and PWM (phytohemagglutinin and poke-weed mitogen) stimulated lymphocytes from males with XLP, their carrier mothers and controls. XLP is a rare lymphoproliferative disorder in which affected males fail to mount appropriate immune responses to Epstein-Barr virus and fatal infectious mono, lymphoma or agammaglobulinemia occur. An increased rate of chromosomal breakage was reported in PHA cultures within one family. Lymphoblastoid cell lines (LCL) from males displayed more chromosomal breakage than LCLs from carrier females. Both the chromosomal aberration frequency and the degree of polyploidy increased with time in culture. This was true of LCLs of males and carriers. The sister chromatid exchange frequencies did not differ between males, carriers, and controls in LCLs, PHA or PWM cultures. The SCE of the cell lines was lower than the PHA or PWM cultures. PWM cultures also had a lower SCE rate than PHA cultures. The low rate of SCE in the transformed cell lines is an intriguing observation. We attempted to use cytogenetic studies as a diagnostic tool for XLP. The relative similarity in chromosomal breakage and SCE frequencies in LCLs of affected males, carrier females and controls may indicate that at the chromosomal level, cells of XLP patients and carriers have similar repair capabilities in response to EBV as do cells from normal individuals. (1 Ref)

22. CHROMOSOMES IN HODGKIN'S DISEASE.

Rowley JD
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Cancer Treat Rep; 66(4):639-643 1982

Chromosome studies in lymph nodes from patients with Hodgkin's disease have been limited by the low yield of dividing cells. Of 25 consecutive involved lymph nodes, 12 had no mitotic cells, 3 had only normal cells, 7 had a mixture of normal and abnormal cells, and 3 had only abnormal cells. Correlating histology with the karyotype, 66% of unsuccessful samples were of the nodular sclerosing type. The majority (58%) of samples with no dividing cells were from previously treated patients. Distinct clones were obtained in samples from only 4 of 10 patients with abnormal cells. Samples from the other six patients had single abnormal cells with bizarre marker chromosomes; these single cells probably represent the only dividing malignant cell. The high failure rate and the low number of clear-cut aneuploid clones in Hodgkin's disease contrast markedly with other lymphomas in which 80% of the samples yield mitotic cells that represent an aneuploid clone in virtually every instance. (Author abstract) (22 Refs)

23. CYTOGENETICS OF MALIGNANT LYMPHOMAS.

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Dtsch Med Wochenschr; 107(12):468-471 1982

Methods and findings of cytogenetic analysis of malignant lymphomas (ML) are reviewed. Analysis consists of counting and structural examination of chromosomes using fluorescence or Giemsa banding techniques. Specific abnormalities characteristic of ML include loss or gain of certain chromosomes, presence of specific chromosomal alterations, and increased frequency of rearrangements of specific chromosomal regions. The most common extra chromosomes found in lymphomas are chromosomes 7, 3, and 12. The most common structural change is the marker 14q+, found in 64% of all lymphomas. Epstein-Barr virus (EBV) apparently is linked to chromosome 14, although the 14q+ marker is also found in EBV-negative lymphomas. Chromosome 14 is apparently involved in control of cell proliferation. Other chromosomes frequently showing alterations in lymphomas are 1, 6, and 11. Chromosome 1 is of particular importance in myeloid lymphomas. Chromosomal rearrangement alters gene function by a position effect. ML cells show a rate of sister chromatid exchange double of that found in normal cells, indicating chromosomal instability. Cytogenetic analysis can be used to differentiate ML from other lymphatic disorders. Staging of ML is aided by detection of chromosomal abnormalities in otherwise apparently normal biopsy tissue. Presence or absence of particular anomalies is of prognostic value, especially in cases of B-cell acute lymphatic leukemia and hairy-cell leukemia. (18 Refs) (In GER)

24. POSSIBLE ORIGIN OF THE REED-STERNBERG CELL FROM AN INTERDIGITATING RETICULUM CELL.

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Dept. Lab. Medicine, Univ. Washington, SB-10, Seattle, WA, 98195
Cancer Treat Rep; 66(4):601-608 1982

In a comparative immunologic and cytochemical analysis, Reed-Sternberg (RS) cells from seven patients with Hodgkin's disease were found to more closely resemble interdigitating reticulum cells (IDC) than normal or malignant histiocytic reticulum cells (macrophages); malignant macrophages were established as a cell line from a patient with malignant histiocytosis. RS cells and IDC both showed strong expression of human Ia-like antigens, a close physical association with helper/inducer T cells, and a lack of at least two common macrophage antigens. Supportive evidence of the identity of RS cells and IDC was their lack of lymphoid and myeloid characteristics, smaller content of nonspecific esterase and acid phosphatase than that in histiocytes, similar cytology, and location in thymic-dependent regions of lymphoid tissues. Malignant transformation of the IDC to an RS cell could result in diminished antigen-presenting capacity and contribute to the defect in T-cell-mediated immunity that commonly occurs in Hodgkin's disease. (Author abstract) (27 Refs)

25. 'PROLYMPHOCYTOID' CELLS IN CHRONIC LYMPHOCYTIC LEUKAEMIA AND THEIR PROGNOSTIC SIGNIFICANCE.

Economopoulos T, Fotopoulos S, Hatzioannou J, Gardikas C
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Scand J Haematol; 28(3):238-242 1982

The morphology of lymphocytes in blood and bone marrow smears from 103 patients with chronic lymphocytic leukemia (CLL) was studied. Special attention was paid to the finding of immature cells with the morphological features of prolymphocytes (prolymphocytoid cells - PLC). Subsequently the prognostic significance of these cells was examined. It was found that in 85 cases no PLC were found (Group I); in 8 cases the percentage was less than or equal to 10% (Group II) and in 10 cases the PLC were greater than 10% (Group III). The cases with PLC, especially in group III, fell in advanced stages of the disease (III-IV) and presented with increased lymphocytosis. In 8 patients of group III, who were followed till death, the disease became refractory to any treatment and the survival was short. We suggest that 'prolymphocytoid' transformation is a bad prognostic sign in CLL. (Author abstract) (8 Refs)

26. ACUTE MYELOID LEUKEMIA WITH HAND-MIRROR CELLS.

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Arch Pathol Lab Med; 106(6):271-274 1982

A retrospective analysis of 37 cases of acute myeloid leukemia (AML) seen during 5 yr was undertaken to evaluate the presence in the bone marrow of hand-mirror cells (HMCs). Three cases with greater than 5% HMC were investigated by light and electron microscopy, cytochemistry, levels of terminal-deoxynucleotidyl-transferase, study of histologic aspects of bone marrow clot and biopsy specimens, and bone marrow immune complexes for numerous viruses. The findings supported the myeloid nature of the HMC; however, immune complexes associated with the baboon endogenous virus were absent, a finding that has been observed in all cases of acute lymphoblastic leukemia (ALL) with HMCs so studied. In light of this finding, it was suggested that HMCs are produced in ALL and AML by different mechanisms. In addition, the patients with AML-HMC did not survive longer than those without HMCs in the bone marrow. Further studies in larger groups are needed to clarify the phenomenon of HMC formation in AML and its relation to survival. (Author abstract) (18 Refs)

27. THROMBOCYTOPENIA AS PRESENTING SYMPTOM OF PRELEUKAEMIA IN 3 PATIENTS.

Tricot G, Criel A, Verwilghen RL
Dept. Medicine, Kapucijnenvoer 33, 3000 Leuven, Belgium
Scand J Haematol; 28(3):243-250 1982

Three patients with preleukemia (idiopathic acquired myelodysplasia) presenting with isolated peripheral thrombocytopenia and an increased number of megakaryocytes are described. The diagnosis of preleukemia, however, was strongly suspected on bone marrow morphology, revealing an abnormal megakaryocytic series. Megakaryoblasts with characteristic nuclei and basophilic pseudopodes, and immature megakaryocytes were frequent. These last cells had 1 or 2 nuclei and a basophilic poorly granulated cytoplasm, often containing large vacuoles, corresponding to dilated interconnecting demarcation membranes in electron microscopy. Megakaryocytes were not considered able to produce a normal amount of platelets, explaining the peripheral thrombocytopenia; platelet survival (51Cr) was indeed too long for ITP. Cytogenetic analysis confirmed the diagnosis of an abnormal hematopoietic clone. Ferrokinetics, in vitro agar cultures, bone marrow biopsy and platelet function tests were helpful additional examinations for establishing the correct diagnosis. It is important to differentiate preleukemia from ITP. Prognosis is totally different and the treatment is not only ineffective in the great majority of the preleukemic patients, but may be hazardous. (Author abstract) (13 Refs)

BIOCHEMICAL, IMMUNOLOGICAL AND OTHER CELL BIOLOGY STUDIES

28. PHORBOL ESTER INDUCTION OF LEUKEMIC CELL DIFFERENTIATION IS A MEMBRANE-MEDIATED PROCESS.

Cooper RA, Braunwald AD, Kuo AL
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Proc Natl Acad Sci USA; 79(9):2865-2869 1982

Phorbol esters are potent inducers of macrophage-like differentiation in the HL-60 promyelocytic leukemia cell line. The sequence of events by which they bring about this transition is poorly understood. However, it is known that phorbol esters bind to the surface membrane of HL-60 cells and to various other cells as well. Our studies were directed toward determining the biologic importance of this membrane association. [3H]Phorbol dibutyrate (PBu2) was specifically bound by HL-60 cells with a Kd of 23 nM and with 1.9 x 10(5) binding sites for [3H]PBu2 per cell. There was no internalization of bound [3H]PBu2. Specific binding was fully reversible upon washing in fresh medium, and [3H]PBu2 added thereafter bound normally to its receptor. Within 10 min of binding, PBu2 stimulated [14C]choline incorporation into phosphatidylcholine, with a rapid return to normal upon removal of the PBu2. Membrane-bound PBu2 progressively inhibited DNA synthesis, with 70% inhibition by 8 hr. This process was interrupted if the PBu2 was removed and little recovery of DNA synthesis occurred in previously inhibited cells. Between 8 and 16 hr, PBu2 induced adherence of cells to plastic, but only in those cells in which phosphatidylcholine synthesis was stimulated, and this process was also interrupted if PBu2 was removed prior to 16 hr. Similarly, nonspecific esterase, which develops after 72 hr of incubation, was induced in cells exposed to PBu2 for the initial 16 hr but not in cells exposed for 5 hr. These studies demonstrate that phorbol esters exert their effects while retained at the cell surface. Inhibition of cell growth and the acquisition of surface and enzymatic properties that characterize macrophages are separable events, even of which proceeds through a receptor-mediated, transmembrane process. The stimulation of phosphatidylcholine synthesis appears to be a part of that process. (Author abstract) (34 Refs)

29. DIFFERENTIATION OF K-562 CELLS: INDUCTION BY THYMOSIN FRACTION 5 (MEETING ABSTRACT)

Ichiki AT, Lozzio BB, Lozzio CB, Bamberger EG
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Fed Proc; 41(3):795 1982

K-562 cells differentiate along the erythrocytic, granulocytic, and monocytic series; hence K-562 cells are considered to be multipotential leukemic cells. These cells express both specific leukemia associated antigens (LAA) and Fc receptors. We initiated a study employing monoclonal antibody preparations to determine the presence of other surface membrane antigens on the K-562 cells. When evaluated with the Cytofluorograf for the binding of F(ab')2 fragment of goat anti-mouse IgG, K-562 cells from 6 or 7 day-old cultures did not bind anti-HLA-A,B,C, anti-HLA-DR, OKT10 (reactive with thymocytes, BM terminal transferase positive cells, BM precursor B cells, and myeloblasts), OKT11 (reactive with large thymic blasts), or anti-monocyte antibody. Over 90% of the cells bound the five monoclonal anti-K-562 antibody preparations of differing specificities. The incubation of cells with thymosin fraction 5 for 24 hours led to changes in the expression of some surface antigens. The number of HLA-A,B,C expressing cells was increased but the number of OKT10 binding cells was only noticeably increased. There was also an increased intensity of the expression of LAA. The fact that the incubation of the K-562 cells with thymosin fraction 5 resulted in the expression of HLA-A,B,C suggests that these cells could be induced to differentiate along the lymphocytic series. (no Refs)

30. INDUCTION OF HEMOGLOBIN SYNTHESIS IN HUMAN ERYTHROLEUKEMIC (K562) CELLS BY ADRIAMYCIN (MEETING ABSTRACT)

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University of Rochester Medical Center, Rochester, NY, 14642
Fed Proc; 41(3):682 1982

The K562 erythroleukemic cell line, isolated from a patient with chronic myelogenous leukemia, has been shown to possess certain erythroid properties, including the expression of glycophorin. In the presence of hemin, K562 cells synthesize fetal and embryonic hemoglobin, but this effect is reversed when hemin is removed from the medium. We have found that adriamycin increases the percentage of hemoglobin-producing K562 cells (as detected by benzidine staining) by a factor of 3 to 5, as compared to untreated cells. This effect of adriamycin appears to be irreversible, since when cells are pulsed with adriamycin for 16 hours and then grown in the absence of adriamycin for 4-5 days, induction of hemoglobin synthesis is still observed. Treatment with adriamycin for 6 hours or less does not induce hemoglobin synthesis. Amiloride and monensin inhibit induction by adriamycin in K562 cells. This may suggest involvement of Na+ and/or Ca++ in the inducton process, as has been suggested for mouse erythroleukemic cells. (2 Refs)

31. UPTAKE INTRACELLULAR DISTRIBUTION AND METABOLISM OF N-N1-DIACETYL-14C-PUTRESCINE (DDAB), A POTENT INDUCER OF FRIEND ERYTHROLEUKEMIA DIFFERENTIATION (MEETING ABSTRACT)

Canellakis ZN, Bondy PK, Gazitt Y
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Fed Proc; 41(3):682 1982

Previous publications have implicated ornithine decarboxylase and the polyamines in the induction of differentiation in Friend erythroleukemia (FL) cells. We now report the uptake and metabolism of DDAB in FL cells induced to differentiate by 10mM DDAB (1uCi/umole). The results indicate a gradual increase during induction in the amount of DDAB taken up by 5x10(7) cells within 24 hours to the cytosol (14.4 n moles), nuclear fraction (5.8 n moles) and membrane fraction (15.8 n moles). Concurrently, there is an increase in the extent of conversion of DDAB into the major metabolites, putrescine, spermidine and spermine. At 24 hours 40% of cytosolic DDAB is metabolized and appears as putrescine (11%), spermidine (15.4%) and spermine (2%). We also detected small amounts of N-Monoacetyl putrescine (2%) and N-acetyl spermidine (1%). (no Refs)

32. CHANGES IN CONTRACTILE PROTEINS DURING DIFFERENTIATION OF MYELOID LEUKEMIA CELLS. II. PURIFICATION AND CHARACTERIZATION OF ACTIN.

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J Cell Biol; 93(2):470-478 1982

A myeloid leukemia cell line, M1, differentiates to macrophage and gains locomotive and phagocytic activity when incubated with conditioned medium (CM) from a fibroblast culture and bacterial endotoxin. To characterize the actin molecules before and after differentiation, the actin was purified through three sequential steps: DEAE-Sephadex A-50, polymerization/depolymerization, and Sephadex G-150 chromatography. The critical concentrations for polymerization were compared under different salt concentrations and temperatures. Results together with the data presented in our previous paper, that D- actin in the crude extract did not polymerize, suggest that an inhibitor for actin polymerization is present in this subline. The kinetics experiment revealed a slower polymerization of untreated M1 and D- cell actins as compared with CM-treated M1 actin. This delayed polymerization was due to a delay during the nucleation stage, not during the elongation stage. By isoelectric focusing, the ratios of beta- to gamma-actin showed a marked difference depending on the states of cells. Tryptic peptide maps also revealed the presence of different peptides. Thus, the functional differences of actin before and after the differentiation was accompanied by some chemical changes in actin molecules. (61 Refs)

33. ESTABLISHMENT AND CHARACTERIZATION OF A HUMAN MYELOMA CELL LINE (KMM-1).

Togawa A, Inoue N, Miyamoto K, Hyodo H, Namba M
Dept. Internal Medicine, Kawasaki Medical Sch., Kurashiki-shi, Japan
Int J Cancer; 29(5):495-500 1982

A new cell line (KMM-1) was established from a subcutaneous plasmacytoma of a 62-yr-old male with multiple myeloma. Immunological studies indicated that cultured cells were derived from the same clone of myeloma cells in vivo: smeared cells were stained with fluorescein-conjugated globulin of antisera monospecific to lambda-chain, and lambda-chains in the cell extracts and in culture media were identical to the Bence-Jones protein found in the patient's urine. The cell line grew in suspension with a doubling time of 36-40 hr and contained primitive plasmablastoid cells with prominent nucleoli and rough endoplasmic reticulum. Cells had the karyotype of 47, X, -Y, Iq+,-2, +t(1:2) (cen:cen), +7, 12q+, 14q+, +mar and carried no Epstein-Barr virus-determined nuclear antigen. Surface markers were as follows; E rosette (-), IgG Fc receptor (-), C3 receptor (-), S-Ig (+), TdT (-), asialo-GM1 (-). The reasons for the successful establishment of the myeloma cell line are discussed. (Author abstract) (23 Refs)

34. HUMAN MYELOMA CELL LINE CARRYING A PHILADELPHIA CHROMOSOME.

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Dept. Hematological Medicine, Cambridge Univ. Clinical Sch., Cambridge CB2 2QL, England
Science; 216(4549):997-999 1982

A new human plasmacytoma cell line (Karpas 707) has been established from a myeloma patient. The culture cells are negative for Epstein-Barr viral nuclear antigen and free of mycoplasma. They are similar to plasma cells and secrete only lambda light chains. The cells are hypodiploid and contain the Philadelphia chromosome and other abnormalities. This cell line must be suitable for the production of human monoclonal antibodies. (Author abstract) (16 Refs)

35. IN VITRO CLONING OF HAIRY CELL LEUKEMIA (HCL) (MEETING ABSTRACT)

Hofmann V, Merchant R, Fehr J, Fruh U, Kiser A, Muller HJ, Martz G
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Proc Am Soc Clin Oncol; 1:C-530 1982

The present report describes the in vitro cloning of hairy cells (HCs) from spleen and/or peripheral blood of 9 HCL patients (pts). Ficoll-separated mononuclear cells (5-100% HCs) either unfractioned or after T-cell depletion with sheep red blood cells were plated at concentrations ranging from 0.1-1.6x10(6)/ml in alpha-MEM (minimum essential medium) containing methylcellulose (1.6%) and leukocyte-conditioned medium (0.2-0.8%) stimulated with phytohemagglutinin for 7 d. Growth was monitored daily: clusters (3-40 cells) became apparent after 48 hr and colonies (40-500 cells) between d 4 and 6. Colonies were round and compact. Up to 10% of cells in colonies incorporated 3H-thymidine when examined autoradiographically. Cytogenetics revealed numerous metaphases. All 9 HCL samples grew with cloning efficiencies of about 0.1%. Peripheral blood from 3 pts with CLL (chronic lymphocytic leukemia) and 2 with Sezary syndrome failed to grow in the same system. Several techniques were applied to prove origin of cells in colonies. Fifty-95% of cells in colonies displayed strong tartrate-resistant acid phosphatase activity. Ultrastructure analysis also confirmed their HCL characteristics. So far, marked cytogenetic abnormality has been found in 1/4 HCL. (no Refs)

36. CLASSIFICATION OF HUMAN LEUKEMIAS BY MOLECULAR HYBRIDIZATION.

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Scott Med J; 27(2):180-182 1982

A recombinant library containing DNA copies of messenger RNA (mRNA) isolated from the buffy coat of a Philadelphia chromosome positive chronic granulocytic leukemia (CGL) patient was prepared and used to distinguish various human leukemias. The autoradiographic patterns observed with preparations from several CGL patients were similar, while very significant differences were observed between CGL and other cell types. (5 Refs)

37. GUANYLATE CYCLASE ACTIVITY IN HUMAN LEUKEMIC AND NORMAL LYMPHOCYTES. ENZYME INHIBITION AND CYTOTOXICITY OF PLANT EXTRACTS.

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Enzyme; 27(3):179-188 1982

Cyclic GMP is thought to be involved in lymphocytic cell proliferation and leukemogenesis. In general, the nucleotide is elevated in leukemic vs normal lymphocytes and changes have been reported to occur during remission and relapse of this disease. Although the cA/cG ratios are higher for normal lymphocytes the basal guanylate cyclase (EC 4.6.1.2) activities do not correlate with altered cyclic GMP levels. The crude guanylate cyclases display classical Michaelis-Menten kinetics with Kms for Mn-GTP of 463 umol/l and 20-90 umol/l for normal and leukemic lymphocytes, respectively. An extract from the bitter melon (momordica charantia) preferentially inhibits the soluble guanylate cyclase from leukemic lymphocytes. This inhibition correlates with its preferential cytotoxic effects for these same cells. Analyses of nine other cytotoxic plants extracts revealed that only an extract from the Lawson's cypress, Chamaecyparis lawsonianna, exhibits comparable cytotoxicity and guanylate cyclase inhibition levels. (Author abstract) (29 Refs)

38. REVERTANT EXPRESSING A STRUCTURAL VARIANT OF T200 GLYCOPROTEIN.

Hyman R, Trowbridge I, Stallings V, Trotter J
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Immunogenetics; 15(4):413-520 1982

The BW5147(T200-a) mutant, a T200-mutant derived from the T200 glycoprotein-positive T-cell lymphoma BW5147, was mutagenized with gamma-irradiation. Thirteen days later 1 x 10(7) cells were stained with 13/2.3 monoclonal T200-specific antibody and fluorescein-labeled goat anti-rat immunoglobulin and sorted for the most fluorescent 0.2% of cells. After the fourth sorting, a detectable antigen-positive population was seen. The antigen-positive cells were split into two groups: line 1 and 2 were the most fluorescent 0.8% and 0.1%, respectively. The two lines were grown up and resorted separately and each line was cloned by limit dilution. Two clones, BW5147 x REV(T200-a) 1.1 and BW5147 x REV (T200-a)2.5, derived from lines 1 and 2, respectively, are described. The structure of the T200 glycoprotein found on the surface of the revertant cell lines was investigated by isolation of the molecule from lysates of radioiodinated cells by immunoprecipitation with monoclonal T200-specific antibody and analysis on polyacrylamide gels. The T200 glycoproteins (mol wt 105,000) isolated from the two revertant clones were much smaller than the wild-type molecule (mol wt 200,000). Results of 21P-labeling and tryptic cleavage and peptide mapping suggested that the major portion of the revertant T200 molecule is in the region of the wild-type molecule external to the plasma membrane. The implications of the such findings are discussed. (18 Refs)

39. IMPLICATIONS OF PERSISTENT T CELL ABNORMALITIES FOR THE ETIOLOGY OF HODGKIN'S DISEASE.

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Cancer Treat Rep; 66(4):681-687 1982

Untreated patients with Hodgkin's disease are known to have significant impairment of cellular immunity. Recent studies have demonstrated that effector T cells from these patients have increased sensitivity to the suppression mediated by two normal immunoregulatory cells, ie, suppressor monocytes and suppressor T cells. Thus, increased sensitivity to suppression may be a common cause of multiple abnormalities of cellular immunity. Patients achieving long-term disease-free survival after chemotherapy have also been studied. Although they are no longer anergic, they have persistent reductions in peripheral blood E rosettes and T cell proliferation. Increased sensitivity to suppressor monocytes and T cells also persists. These abnormalities do not appear to be caused by the treatment since they were not detected in diffuse histiocytic lymphoma patients surviving after similar chemotherapy. Immunologic studies in family members are required to determine whether these abnormalities are a permanent immunologic deficit acquired only with the development of Hodgkin's disease or an inherited characteristic that predisposes a patient to develop Hodgkin's disease. (Author abstract) (22 Refs)

40. DEFICIENT HELPER T CELL ACTIVITY IN NON-HODGKIN'S LYMPHOMAS (MEETING ABSTRACT)

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Proc Am Assoc Cancer Res; 23:991 1982

The observations that lymphomas are more common 1) after organ transplantation and immunosuppressive therapy, and 2) in certain autoimmune diseases suggest that altered immunoregulation may play a role in lymphoma pathogenesis. Thus, we investigated regulatory T cell function in the peripheral blood in 13 untreated adult non-Hodgkin's lymphoma patients and 13 age and sex matched controls. Six patients had nodular lymphomas, 7 diffuse. Nine had B cell tumors. No known T cell tumors were studied. Control mononuclear leukocytes (MNL) had greater proliferative responses to pokeweed mitogen (PWM) than patient MNL. MNL were separated into T and non-T fractions by two sequential neuraminidase-E-rosette sedimentations. Non-T cells were unresponsive to PWM. Responses of normal and patient T cells were similar. When normal non-T and autologous irradiated (3000R) T cells were cocultured, the response exceeded the response of patient non-T and autologous irradiated T cocultures. When normal non-T cells were cocultured with patient irradiated T cells, their response was diminished. Moreover, when patient non-T cells were cocultured with normal irradiated T cells, their response was enhanced. Normal non-T cell responses were the same regardless of whether autologous or normal allogeneic irradiated T cells were used as helpers. These results suggest that peripheral blood T cells from patients with non-Hodgkin's lymphoma

are deficient in helper capacity for non-T cell blastogenic response to PWM and that patient non-T cells may have a normal proliferative response in the presence of normal allogeneic (helper) T cells. Abnormal immunoregulatory cell function may be important in the pathogenesis of the non-Hodgkin's lymphomas. (no Refs)

41. INHIBITORY EFFECTS OF VARIOUS OXYGENATED STEROLS ON THE DIFFERENTIATION AND FUNCTION OF TUMOR-SPECIFIC CYTOTOXIC T LYMPHOCYTES.

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Transplantation; 33(5):482-491 1982

These studies were undertaken to determine the effect of various oxygenated sterols (representing a number of known cholesterol-derived photoproducts) on the generation (afferent) and function (efferent) of cytotoxic T lymphocytes (CTLs). Cell-mediated immune responses which result in the generation of both alloantigen-specific and syngeneic tumor-specific CTLs were evaluated. The results of our studies established the following points: (1) the afferent phase of an immune response is particularly sensitive to the effects of some cholesterol photoproducts while other oxidized sterol derivatives, known to exist in skin following UV light (UVL) exposure, have minimal influence on the generation of CTL responses; (2) the only known carcinogenic photoproduct of cholesterol (cholesterol alpha-oxide) is a very weak inhibitor of lymphocyte function; and (3) presentation of oxygenated sterols via liposome membranes is 10-fold more effective than their administration in soluble form; (4) 25-hydroxycholesterol and 20alpha-hydroxycholesterol were found to be the most potent inhibitors, causing a parallel depression in lymphocyte proliferation, CTL activity, and endogenous sterol biosynthesis, and (5) 7beta- and 7alpha-hydroxycholesterol functioned in a unique manner, causing an abrogation of CTL activity without depressing proliferative responses and endogenous sterol biosynthesis to a significant degree. These studies represent the first time that an attempt has been made to evaluate a possible biochemical basis for immune suppression known to precede experimental UVL carcinogenesis. Our results suggest that some, but not all, of the oxidation products of cholesterol found in skin following UVL irradiation exert an influence on immune responses. Derivatives of cholesterol could be partially responsible for the alterations in immunological potential of the UVL-exposed host. The induced presence of an inhibitor of CTL differentiation or function at a time following UVL tumor emergence may play a role in this process by providing an early tumor escape mechanism. (37 Refs)

EXPERIMENTAL STUDIES INVOLVING CHEMICAL AGENTS AND IRRADIATION

42. EFFECTS OF 7,12-DIMETHYLBENZ(A)ANTHRACENE ON THYMUS CORTEX IN THE RAT. A MORPHOLOGICAL AND HISTOMETRICAL ANALYSIS.

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Virchows Arch [Cell Pathol]; 39(2):125-136 1982

In the rat, administration of 7,12-dimethylbenz(a)anthracene (DMBA) causes necrosis of the inner layers of the adrenal cortex and provokes rising levels of plasma cortisol. Histological and ultrastructural study of the thymus demonstrates a profound depletion of small thymocytes, especially in the inner cortex where they normally represent the greater part of the cell population. The thymic weight, and the cortico-medullary ratio as measured by histometry, decrease significantly. These findings are similar to those observed following steroid administration. However, whereas after steroid treatment restitution of the normal complement of thymocytes occurs within 7-10 days, in the present model the thymic weight and cortico-medullary ratio remain at the low levels observed on Days 1 and 3 until after Day 24 following DMBA administration. A block in the regenerative process is confirmed by the results of morphometrical analysis of the thymocyte nuclear area in the cortex. On Day 1 and 3 after DMBA the mean thymocyte nuclear area is reduced in the outer cortex and increased in the inner cortex, because of the selective destruction of small thymocytes and the migration of the corticoresistant blast thymocytes towards the medulla. Subsequently, until after Day 24 the mean nuclear area of the thymocytes is significantly higher in the outer and in the inner cortex of treated rats than in the corresponding parts of the cortex of control rats. This aspect of the cortex is characteristic of the early phase of the regenerative process, ie of Day 2 or 3 after steroids administration. It can be assumed that in this experimental mode the thymic changes are due not only to the raised cortisol level but also to a direct effect of DMBA on the thymus, which is probably an inhibition of DNA synthesis in cells in the S phase of the mitotic cycle, ie in the replication of DNA. It also seems possible that a causal relationship exists between inhibition of DNA synthesis in proliferating organs like the thymus, and the carcinogenic activity of DMBA. (Author abstract) (35 Refs)

43. INCIDENCE AND TYPE OF TUMORS INDUCED BY ORAL DMBA IN NK CELL DEFICIENT C57BL BG/BG MICE, +/BG LITTERMATES AND H-2 CONGENIC STRAINS OF B10 OF VARYING NK ACTIVITY (MEETING ABSTRACT)

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9th International RES Congress, February 7-12, 1982, Davos, Switzerland. American Reticuloendothelial Society 68 pp., 1982.

To study the effect of the beige mutation on chemical carcinogenesis, 64 C57Bl bg/bg mice and 83 +/bg littermate controls received 5 weekly intragastric doses of DMBA (dimethylbenzanthracene). We examined the incidence and histological types of tumors that developed. By 165 days after first DMBA contact 18% of +/bg, and 31% of bg/bg mice developed tumors. Beige mice had a higher incidence of epithelial and non-epithelial tumors in cutaneous or subcutaneous sites. The incidence of lymphomas was similar in the groups but they appeared earlier in the beige. After 500 days 33 +/bg and 27 bg/bg mice were still alive, 60 of 83 +/bg animals (72%) and 47 of the 64 bg/bg (74%) having developed tumors. The beige group showed a higher incidence of non-thymic lymphomas, but the incidence of thymic lymphomas, cutaneous epithelial tumors and bile duct adenomas was similar in the two groups. In a continuing study of NK intact B10 (27), B10A (25), B10.BR (39), B10G (48) mice and NK cell deficient B10S congenic animals (30), squamous carcinomas have developed more frequently in B10S animals (B10S 8/30-27%) rest (11/139-8%, P less than 0.05). At present it looks as though both thymic and extra thymic lymphomas may also be of increased frequency in the B10S, NK deficient animals. The role of DMBA as a suppressor has been confirmed. (no Refs)

44. THE CARCINOGENESIS OF B LYMPHOCYTES IN PEYER'S PATCHES OF RATS (MEETING ABSTRACT)

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Fed Proc; 41(3):553 1982

Spontaneously arising B cell leukemias in experimental animals are rare. Furthermore the experimental protocols used to induce lymphoid malignancies seemingly have little efficacy in the induction of malignancies of B cell origins. Therefore a different approach was used in the study reported here. The basic procedure was to localize a chemical carcinogen in the Peyer's patches of rats which were previously treated with anti-IgD to induce B cell proliferation in vivo. Thus far 9 of 15 3-methylcholanthrene (MCA) and 4 of 14 7,12-dimethylbenzanthracene (DMBA) treated rats have developed lymphoid malignancies which have been characterized, based on morphology, growth kinetics, pathogenesis and cell surface markers, as: 1) B cell chronic lymphocytic leukemias which coexpress membrane IgM and IgD (3 MCA treated rats), 2) Immature B cell leukemias which preferentially express membrane and/or cytoplasmic IgM (3 MCA treated rats), 3) B cell nodular lymphomas with immunoblastic characteristics (3 MCA and 1 DMBA treated rats) and 4) T cell thymomas (3 DMBA treated rats). Studies have also been done to propagate the B cell malignancies in vivo and in vitro. These studies indicate that the treatment of Peyer's patches with chemical carcinogens may provide a selective means of inducing B lymphocytic malignancies. (no Refs)

45. CHARACTERIZATION OF A LYMPHOMA INDUCED BY BUSULFAN AND CHLORAMPHENICOL IN CAF1 MICE (MEETING ABSTRACT)

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Fed Proc; 41(3):410 1982

We previously showed that injection of Busulfan and chloramphenicol into CAF1 mice induced the development of T-cell lymphoma in 50% of mice. The lymphoma cells were transplantable into other CAF1 mice by subcutaneous injections. In the recipients the leukemic cells grew as a subcutaneous nodule with late infiltration of the spleen. The cells from the nodule expressed Thy 1.2 alloantigen, brain associated antigen on 90% and Lyt 2.2 antigens 58% of the cells. They were negative for Lyt 1.1, 2.1, 1.2 and Ia antigens. The primary immune response to sheep erythrocytes were measured in these mice by hemolytic plaque assay. The sheep cell immune response was normal when compared to age matched control, but depended on the state of the splenic infiltration. The complete infiltration of the spleen diminished the response but with partial infiltration the response was intact. The cells from the nodule were negative for plaque forming cells. These studies indicate that the lymphoma induced by Busulfan and chloramphenicol are transformed T cells which did not interfere with primary sheep cell immune response in the lymphoma mice. (no Refs)

46. HISTOPATHOLOGY OF HALOTHANE ASSOCIATED MURINE LYMPHOMAGENESIS (MEETING ABSTRACT)

Cruse JM, Lewis RE, Johnson W, Mohammad A
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Fed Proc; 41(3):335 1982

The present investigation was designed to demonstrate whether exposure of autoimmune and lymphoma-prone BXSB/Mp male mice to halothane could facilitate premature onset of lymphomagenesis compared to mice not exposed to halothane that develop the lymphoma-like disease naturally. No morphologic evidence of onset of lymphoma-like disease was observed in our 12-14 week-old BXSB/Mp male mice. Nor was there any morphologic evidence of disease onset at 12-14 weeks of age with only one exposure of halothane. The earliest morphologic evidence of lymph node disease was at 14-16 weeks of age with 5 exposures to halothane. There was increasing lymph node involvement accompanied by loss of architecture corresponding approximately to the number of halothane exposures. The earliest morphologic change in lymph nodes from halothane-treated BXSB/Mp male mice consisted of increased numbers of plasmacytoid cells which infiltrated the medullary cords. More advanced stages revealed both medullary cord and sinusoidal involvement with paracortical infiltration and finally obliteration of the cortical and medullary architecture of the entire lymph node. Nuclear size varied with 2 or 3 eosinophilic nucleoli in larger nuclei. The largest infiltrative cells had cytologic characteristics of immunoblasts. Although lymph nodes from control BXSB females showed hyperplasia of lymphoid follicles, none showed the lymphoplasmacytoid infiltrative, architecturally obliterative pattern found in males with the disease. (no Refs)

47. SPONTANEOUS REGRESSION OF CHEMICALLY INDUCED TRANSPLANTABLE LEUKEMIA IN C3H/HE-MG MICE (MEETING ABSTRACT)

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VI Meeting of the European Association for Cancer Research, October 12-15, 1981, Budapest, Hungary. The European Association for Cancer Research 275 pp., 1981.

Acute lymphatic leukemia has developed in a male/AKRxC3H/F1 mouse treated with urethane and diethylstilbestrol (DES). This leukemia was transplanted by the authors into female and male C3H/He-mg mice. In newborn mice generalized lymphatic leukemia developed which killed the animals. In addult female mice generalized lymphatic leukemia developed that killed them in two weeks, too. On the other hand in adult male animals such a kind of lymphoma developed that regressed spontaneously in about 3 weeks. The fact of spontaneous regression was proved by histology, enzymatic examinations and flow-cytometric analyses. The phenomenon is similar to the spontaneous regression of Gross-virus leukemia observed in C3H/He-mg mice. The regression was proved in identical ways. It can be stated that pyruvate-kinase (PK) enzyme marker may adequately be applied to follow the progression and regression of leukemia and the alteration in the PK activity correlates with the volume of cells and the histological results. (no Refs)

48. COMPARATIVE BIOCHEMICAL STUDIES ON CHEMICALLY INDUCED TRANSPLANTABLE LEUKEMIAS (MEETING ABSTRACT)

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VI Meeting of the European Association for Cancer Research, October 12-15, 1981, Budapest, Hungary. The European Association for Cancer Research 275 pp., 1981.

Leukemias, histologically differing both from each other and from Gross-virus leukemia, were originally induced by urethane or urethane + diethylstilbestrol in C3HxAKR/P1 hybrid

mice. The O2 consumption, lactic acid production and hexokinase, phosphofructokinase, pyruvate kinase, lactic acid dehydrogenase and thymidine kinase activities of the leukemic mesenteric lymph nodes were compared both with each other and with those of Gross leukemic lymph nodes and normal controls. The investigated parameters were found to be characteristic of the individual types of leukemias. They are probably suitable markers for the differentiation between these leukemias. (no Refs)

49. MYELOGENOUS LEUKEMIA IN THE RF MOUSE.

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Am J Pathol; 107(2):280-284 1982

Sequential development of hematologic and pathologic events was examined for up to 6 mo after irradiation in RF/J male mice. Such mice show a high incidence of myelogenous leukemia (ML) following irradiation. One wk after exposure to 425 rads, treated animals showed slightly lowered RBC and significant depression of WBC. Detection of increased numbers of WBC was followed by death within 7-14 days. Spleen, liver, and thymus tissues from sacrificed animals and those dying of leukemia showed a disease incidence of 62% in animals surviving 10 wk or longer. In another experiment, animals were sacrificed at 4-wk intervals after radiation exposure. At 12 wk after irradiation 3/5 animals had histologic changes consistent with early ML. The time sequence of morphological and clinical changes is described. Radiation-induced ML in RF/J mice is compared with human ML. The usefulness of the RF/J mouse ML model is considered. (14 Refs)

EXPERIMENTAL STUDIES: DNA TUMOR VIRUSES

50. A MURINE MODEL SYSTEM FOR STUDYING THE MOLECULAR MECHANISM OF EPSTEIN-BARR VIRUS (EBV)-MEDIATED CELL TRANSFORMATION AND CARCINOGENESIS (MEETING ABSTRACT)

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Fed Proc; 41(3):688 1982

EBV can normally infect in vitro only human and marmoset B lymphocytes, leading to cell transformation without any primary viral reproductive cycle. Using our method of EBV receptor-implantation we demonstrated that any other cell which is artificially provided with EBV receptors can be infected by the virus. Here we show also that EBV receptor-implanted mouse lymphocytes are infectible by EBV, when using either the transforming B-95-8 (B-EBV) or non-transforming P3HR-1 (P-EBV) substrains of the virus. Unlike the natural host, mouse lymphocytes are not readily transformed by B-EBV. Instead, the cells support a full viral lytic cycle, resulting in the release of a new biologically active EBV isolate (M-EBV). Unlike the natural host, the EBV-infected mouse cells express the virus-determined early (EA) and virus capsid (VCA) antigens. Suprisingly, the EBV-nuclear antigen (EBNA) is barely detectable. This model system is used to test the hypothesis that the EBV-related oncogenic mechanism involves a virus-mediated increase in intracellular proteins, presumably as a complex between a virus coded 48,000 dalton component and a cell-coded 53,000 dalton component, which may block the viral lytic cycle and interfere with cell differentiation leading to transformation. (no Refs)

51. CHARACTERIZATION OF IMMUNOGLOBULIN SECRETION BY BURKITT'S LYMPHOMA (BL) CELL LINES (MEETING ABSTRACT)

Benjamin D, Magrath IT, Maguire R, Weiss RB, Blaese M
National Cancer Institute, Bethesda, MD, 20205
Proc Am Assoc Cancer Res; 23:1026 1982

As part of an investigation of the cellular origins of undifferentiated lymphoma (UL) we have studied immunoglobulin (Ig) secretion in cell lines derived from American (AM) and African (AF) BL, Epstein Barr Virus (EBV) transformed cord blood lymphocytes (CBL) and diploid lymphoblastoid cell lines. Ig secretion was monitored by pulse labelling with either 35S-methionine (Me) or 3H-Leucine (Le) followed by immunoprecipitation with polyvalent anti-human Ig antiserum. Twelve of 14 of AM lines secreted exclusively IgM of a single light chain (LC) class but AM lines secreted greater amounts. Nontumor lines secreted multiple heavy and LC classes. Some lines secreted Ig LC which did not contain Me, but was detected by labelling with Le. A significant correlation between the presence of EBV genome and the absence of Me in the secreted Ig was found. Ten of 11 EBV negative lines secreted Me containing LC whereas Me was not detected in 4/5 EBV positive lines. The IgM in the supernatant had a high M Wt consistent with a pentameric structure and was associated with J chain; features of secreted Ig but not of membrane bound Ig. Free LC were secreted in large amounts in AM lines in contrast to the low amounts detected in AF lines and CBC. Kinetic studies using a Reverse Hemolytic Plaque assay technique have shown that peak of Ig secretion is on the 2nd day after subculturing and only 1% of the cells secrete Ig. Addition of pokeweed mitogen and irradiated B plus T cells or 12-O-Tetradecanoylphorbol 13-Acetate (TPA) induced up to 10 fold increase of Ig secretion in the Am lines. (no Refs)

52. A HETEROANTISERUM AGAINST AMERICAN BURKITT'S LYMPHOMA (BL) (MEETING ABSTRACT)

Magrath IT, Parsons RG
Pediatric Oncology Branch, National Cancer Institute, Bethesda, MD, 20205
Proc Am Assoc Cancer Res; 23:1039 1982

We have raised a goat antiserum (B75) against purified membrane from an American BL cell line and examined its spectrum of reactivity after extensive absorption with either 5 African BL cell lines or 6 Epstein Barr Virus-transformed cord blood lymphocyte (CBL) cell lines. Both methods of absorption yielded antisera with identical specificities. Eleven of 12 EBV genome-negative cell lines derived from American BL (6) and undifferentiated non-BL (6) reacted with B75 using indirect immunofluorescence. Three of 4 EBV genome-positive American undifferentiated lymphomas were also positive, but none of 13 CBL lines or 8 non-tumor lymphoblastoid cell lines reacted with B75. Two of 7 African BL cell lines reacted positively. These 2 lines also secreted small amounts of IgM, whereas none of the 5 negative lines did so. B75 did react with blast cells derived from common acute lymphoblastic leukemia (ALL) but not with blast cells from T-cell ALL or lymphoblastic lymphoma. B75 reactivity persists after incubation of cells with proteolytic enzymes and we have so far been unable to immunoprecipitate a protein from cell lysates with B75. These data indicate that BL cells express one or more antigens

not present on other lymphoid cell lines of normal and neoplastic origin. These data are consistent with the hypothesis that American-BL and undifferentiated lymphoma are the neoplastic counterparts of cell types early in the B-cell pathway, probably immediately after the pre-B cell stage, and before the normal counterpart of African BL. (no Refs)

53. HERPESVIRUS SAIMIRI-INDUCED LYMPHOMA IN NEW WORLD PRIMATES: TUMOR CELL PHENOTYPE AND VIRUS DISTRIBUTION IN T CELL SUBSETS (MEETING ABSTRACT)

Neubauer RH, Klein RA, Briggs C, Rabin H
National Cancer Institute, Frederick Cancer Research Facility, Frederick, MD, 21701
Fed Proc; 41(3):271 1982

Studies using monoclonal antibodies have indicated that the human determinants for the sheep erythrocyte receptor (OKTIIa), the helper/inducer T cell marker (leu3a), and HLA-DR (Ia) antigens are conserved among primates. Using these antibodies and fluorescence activated cell sorter analysis, we examined the phenotype of Herpesvirus saimiri-induced lymphomas in New World primates. Results with owl monkeys or marmosets showed that cell lines established from tumors were uniformly OKTIIa+ and Ia+ and that the cells could be either leu3a+ or leu3a-; mixed cultures were never observed. In contrast, cell lines of normal T cells were comprised of both leu3a+ and leu3a- cells. Twenty-five percent of owl monkeys inoculated with H saimiri develop a disease-free chronic infection where the virus is associated with the T cells. We examined four such animals to determine if the virus is restricted to a specific T cell subset. Virus was restricted to leu3a+ cells in one animal while in other monkeys it was found equally in leu3a+ and leu3a- populations. Studies designed to look at the phenotype and the localization of virus in fresh tumors are in progress. (no Refs)

EXPERIMENTAL STUDIES: RNA TUMOR VIRUSES

54. AMPLIFIED EXPRESSION OF MURINE LEUKEMIA VIRUS (MULV)-CODED ANTIGENS ON THYMOCYTES AND LEUKEMIA CELLS OF AKR MICE AFTER INFECTION BY DUALTROPIC (MCF) MULV.

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Virology; 119(2):450-464 1982

Recently, we have shown that several isolates of recombinant, dualtropic (MCF) murine leukemia virus (MuLV) can induce amplification of MuLV gag and env gene-coded antigens on thymocytes of young AKR mice and, subsequently, can accelerate leukemia in these same animals. With respect to env gene-coded antigens, it is unclear whether antigen amplification represents expression of env gene products of the input virus on the surface of infected thymocytes or whether infection by MCF viruses induces the expression other endogenous env gene sequences. Infection by antigenically marked viruses has allowed us to decide between these alternatives. We have found that AKR MCF isolates 69L1, 13, and 247 can be distinguished serologically by specific patterns of reactivity with mouse and rat monoclonal antibodies that recognize 10 distinct epitopes (single antigenic determinants) of AKR ecotropic MuLV gp70 and p15(E) proteins. Accordingly, 1-mo-old AKR mice were injected intrathymically with either MCF 69L1, MCF 13, or MCF 247 viruses and thymocytes of virus-injected mice were then assayed for amplification of specific epitopes at 32-36 days postinjection. Quantitative expression of MuLV antigens was determined by flow microfluorometry using a fluorescence-activated cell sorter. The patterns of reactivity with monoclonal antibodies which were originally determined for each virus in vitro were found to breed true on thymocytes infected in vivo. Moreover, the phenotype of virus recovered in vitro from virus accelerated leukemias was identical to that of the injected virus. Thus, the preleukemic change of MuLV antigen amplification appears to represent expression on thymocytes of env gene products encoded by the infecting MCF viral genome which continues to be expressed in the resulting leukemias without apparent changes in the recombinant env gene. (Author abstract) (36 Refs)

55. ECOTROPIC MURINE LEUKEMIA VIRUS DNA CONTENT OF NORMAL AND LYMPHOMATOUS TISSUES OF BXH-2 RECOMBINANT INBRED MICE.

Jenkins NA, Copeland NE, Taylor BA, Bedigian HG, Lee BK
Jackson Lab., Bar Harbor, ME, 04609
J Virol; 42(2):379-388 1982

BXH-2 recombinant inbred mice spontaneously produce a B-tropic murine leukemia virus (MuLV) beginning early in life and have a high incidence of non-T-cell lymphomas. These traits are not characteristic of the progenitor strains (C57BL/6J and C3H/HeJ) or of 11 other BXH recombinant inbred strains. Since B-tropic virus expression may be causally related to the high incidence of lymphoma in this strain, we have analyzed the ecotropic MuLV DNA content of both normal and lymphomatous tissues of BXH-2 mice. Southern analysis and hybridization with an ecotropic MuLV DNA-specific probe showed that DNA of normal BXH-2 tissues contained both parental N-tropic MuLV proviruses but lacked endogenous B-tropic MuLV DNA sequences. In addition, none of 116 F1 hybrid mice derived from male BXH-2 mice spontaneously produced ecotropic MuLV early in life. These results suggest that the B-tropic virus is horizontally transmitted in BXH-2 mice. Southern analysis of DNA from tumor tissues of 12 BXH-2 mice showed that amplification of ecotropic-specific DNA sequences had occurred in lymphomatous tissues of 3 mice and suggested that these tumors were monoclonal. The number of newly acquired proviruses, which appeared to be structurally nondefective and integrated at different sites, varied from one to three copies. Since lymphomatous tissues, from only 3 of 12 mice examined carried additional detectable ecotropic proviruses, these results suggest that amplification of ecotropic MuLV DNA sequences is not required for maintenance of transformation in BXH-2 lymphomas. (Author abstract) (36 Refs)

56. THE FUNCTIONAL CHARACTERIZATION OF MALIGNANT LY 1+ T CELL CLONES ISOLATED FROM B CELL LYMPHOMAS (MEETING ABSTRACT)

Sing AP, Morgan N, Reinisch CL
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Fed Proc; 41(3):478 1982

C57Bl/6 mice develop plasmacytoid lymphocytic lymphomas 2 years after injection with MSV-MuLV-Moloney. Cells from the mesenteric lymph node (MLN), unseparated spleen cells or splenic B cells injected into normal B6 mice proliferate

in the MLN and spleen causing B cell lymphomas in 3-4 months. Cells from the lymphoma cell population were cloned at limiting dilution (0.3 cells/well) in the absence of TCGF on a syngeneic feeder layer to establish a series of clonally derived lines. Thus far, 8 clones, designated MSV-LN-AS 1-8 have been generated from individual MSV infected mice; when analyzed with monoclonal antibodies, the cells express the Ly1 and Thy 1.2 differentiation antigens. They are Ly2-, Qa2-and Ig-. Cells isolated from B6 mice injected with malignant lymphoma cells and cultured similarly are also Ly1+Ly2-Thy 1.2+Qa2-Ig-. As few as 1 x 10(6) Ly1+ T cells from the MSV-AS series injected into normal B6 mice cause immunoblastic T cell sarcomas which kill the recipient in one week. Functional characterization of one clone shows that the cells enhance IgM and IgG responses to SRBC in vivo, potentiate specific CTL reactivity to alloantigen in vivo and stimulate Ig secretion by B cells in vitro. These experiments show: 1) a series of Ly1+ T cell clones have been isolated from B cell lymphomas 2) the T cell clones are highly malignant and phenotypically identical and 3) the clones interact with B or T cells to potentiate immune responsiveness. (no Refs)

57. RAPID THYMOMAS INDUCED BY ABELSON MURINE LEUKEMIA VIRUS.

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Proc Natl Acad Sci USA; 79(9):2917-2921 1982

Abelson murine leukemia virus (A-MuLV) is derived from the thymotropic Moloney leukemia virus. However, injection of mice with A-MuLV conventional routes results in rapidly arising peripheral and bone marrow lymphomas, not thymomas or T cell tumors. In this study thymomas have been induced by intrathymic injection of A-MuLV into BALB/c and C57BL/Ka mice. In both strains thymomas arose with short latent periods, comparable with the latencies of nonthymic tumors induced by intraperitoneal injection of A-MuLV and significantly shorter than those of thymomas induced by intrathymic injection of Moloney leukemia virus. Cells of the BALB/c thymomas were predominantly Thy-1-; those of C57BL/Ka thymomas were predominantly Thy-1+. Tissue culture lines were established and cloned. Some of these expressed low amounts of Thy-1 and one also expressed Lyt-1. Virus from cloned lines transformed 3T3 cells in vitro and induced Abelson disease in vivo when injected intraperitoneally into neonates. The A-MuLV p120 protein has been precipitated from metabolically labeled cell lysates of one cloned Thy-1+ line. These results show that A-MuLV can transform cells in the T-lymphocyte lineage. (Author abstract) (22 Refs)

58. GENETIC CONTROL OF THE ANTIBODY RESPONSE TO MURINE LEUKEMIA VIRUSES (MEETING ABSTRACT)

Brown MA, Green WR, Nowinski RC
Fred Hutchinson Cancer Research Center, Seattle, WA, 98104
Fed Proc; 41(3):295 1982

The genetic control of antibody response to proteins of murine leukemia viruses was investigated. Since the antibody response to ecotropic gp70 envelope protein has previously been shown to be linked to the H-2 complex in mice by segregation analysis, more precise mapping was carried out using a panel of B10 congenic mice immunized with AKR ecotropic MuLV. Sera from immunized mice were tested in a radioimmune precipitation assay and the specificity of antibodies demonstrated by polyacrylamide gel electrophoresis. The results confirm that genes within the H-2 complex of mice control the ability to respond to ecotropic gp70. Mice of the H-2b and H-2d haplotypes were responders and mice of the H-2R haplotype were non-responders. The response was dominant in F1 crosses between responder and non-responder parents. Preliminary results employing a series of B10 H-2 recombinant mice have mapped the gene to the I-B region. Control of the antibody response to other viral component proteins such as the p30 core protein was also influenced by H-2 region genes but there was no correlation between the ability to respond to p30 and the ability to respond to gp70. These results were in contrast to the genetic control of response to xenotropic viral proteins. Control of antibody response to xenotropic gp70 was not linked to H-2 and response was recessive in F1 crosses. These findings suggest that different mechanisms may operate in the generation of immune response to ecotropic and xenotropic viral proteins. (no Refs)

59. THYMIC EPITHELIUM DETERMINES PRELEUKEMIC CELLULAR AND VIROLOGICAL CHANGES IN LEUKEMIA-SUSCEPTIBLE MICE (MEETING ABSTRACT)

Zielinski C, Datta S, Waksal S
Department of Medicine II, University of Vienna, Vienna, Austria
12th Workshop on Leukocyte Cultures, February 14-17, 1982, Vienna, Austria Wiener Medizinische Akademie; :A64 1982

Although leukemia-resistant (AKRxNZB)F1 mice (ANF1) inherit dominant genes for the expression of ecotropic and xenotropic viruses, they do not express these retroviruses on their thymocytes. Prothymocytes of ANF1 did express high levels of retroviruses, however, when they differentiated in the thymi of lethally irradiated leukemia-susceptible AKR mice, but not in other 'low leukemia' strain recipients. Furthermore, prothymocytes of leukemia-resistant ANF1 which had differentiated in grafted irradiated AKR thymi expressed murine leukemia virus antigen and certain surface phenotype changes regarding thymocyte differentiation markers as they were observed to go along with increased murine leukemia virus antigen expression in ANF1 to AKR bone marrow chimeras. No increased murine leukemia virus antigen expression was observed on thymocytes of ANF1 to ANF1 thymus graft chimeras. These experiments suggest that murine leukemia virus antigen expression may occur in a specific thymic environment which further leads to shifts in the expression of thymocyte differentiation markers and finally to the development of leukemia. (no Refs)

60. ML ANTIGEN OF DBA/2 MOUSE LEUKEMIAS: EXPRESSION OF AN ENDOGENOUS MURINE MAMMARY TUMOR VIRUS.

Racevskis J, Sarkar NH
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J Virol; 42(3):804-813 1982

Spontaneous, transplantable leukemias of DBA/2 mice express an antigen (ML) which cross-reacts with antigens of murine mammary tumor virus (MuMTV). The MuMTV cross-reactive antigen of the DBA/2 leukemias (ML cells) was found to be a glycoprotein of 78,000 mol wt containing antigenic determinants of the major MuMTV glycoprotein gp52. No MuMTV particles were produced by the ML cells, although they did contain type A particles - the pronucleocapsids of MuMTV. The ML antigen appeared to be an aberrant form of the intracellular MuMTV env precursor molecule prgp70, which was not processed properly but instead acquired extra

carbohydrate groups and was expressed in uncleaved form on the cell surface. Isolation of MuMTV core protein p28 from the leukemic cells and subsequent tryptic peptide mapping analysis showed that the p28 from leukemia cells differed from the p28 of MuMTV isolated from DBA/2 mouse milk. These observations indicate that the MuMTV expressed in DBA/2 leukemic spleen cells is of a different strain than the virus secreted in lactating mammary glands of DBA/2 mice and probably represents the expression of an endogenous DBA/2 provirus. (Author abstract) (34 Refs)

61. GENE REGULATION AND ONCOGENESIS BY RETROVIRUSES (MEETING ABSTRACT)

Varmus HE
Department of Microbiology and Immunology, University of California, San Francisco, CA
Thirty-fifth Annual Symposium on Fundamental Cancer Research, March 2-5, 1982, Houston, Texas. The University of Texas M. D. Anderson Hospital and Tumor Institute 38 pp., 1982.

We studied the functional capacities of long terminal repeats (LTRs) by constructing recombinant plasmids, which contain LTRs and cloned genes in various arrangements, and then introducing them into cultured cells. As expected, only an LTR in the correct transcriptional orientation upstream from a promoter-less gene can produce expresson of that gene. However, when the gene carries its own promoter, the efficiency of DNA transformation is enhanced manyfold by the presence, in either orientation, of certain LTRs suggesting that some LTRs may enhance gene expression at distant, heterologous promoters in a nonpolar fashion. The LTR of mouse mammary tumor virus (MMTV) governs expression of viral or linked cellular genes in a glucocorticoid-responsive manner; the region responsible for hormonal regulation has been localized to about 0.4 kb near the 3' end of the MMTV LTR. The induction of B-cell lymphomas by avian leukosis virus (ALV) appears to require insertion of proviral DNA near c-myc, a putative cellular oncogene. The viral inserts, sometimes comprising little more than a single LTR, can enhance expression of c-myc in at least three arrangments: When positioned upstream from c-myc in the same transcriptional orientation, the inserts are promoters for the transcription of c-myc; when positioned upstream in the opposite orientation to c-myc or downstream in the same orientation, they enhance expression from unidentified cellular promoter(s). In the last instance, the LTR provides a novel site for polyadenylation. Interrupted c-myc loci have been cloned from tumor DNA and reintroduced into cultured cells to identify determinants of the enhancement phenomena. (no Refs)

62. DIFFERING POPULATIONS OF INTRACISTERNAL A-PARTICLE GENES IN MYELOMA TUMORS AND MOUSE SUBSPECIES.

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J Virol; 42(2):411-421 1982

Intracisternal A-particle genes form a family of endogenous retrovirus-like genetic elements that are transcribed in mouse plasmacytomas (myeloma tumors). Two types of A-particle genes that can be differentiated by a sequence of 0.5 kilobase found in one type but not the other have been identified. Quantitative Southern blot analysis was used to measure the populations of different A-particle genes in DNAs from BALB/c mice, the Japanese subspecies Mus musculus subsp molossinus, and myeloma tumors. The majority of the genes (715 copies per haploid genome or 76%) were found to be nearly identical except for small changes in conserved restriction enzyme sites. The second type of A-particle gene was much less abundant with 90 copies representing approx 10%. The A-particle RNA in MOPC104E and MOPC315 was found to be colinear with a small portion of this latter type, comprising only 2% of the endogenous intracisternal A-particle sequences. Myeloma tumor DNA was found to have a two- to fourfold increase in the number of these genes, suggesting that the intracellular viruses have been activated to produce a double-stranded complementary DNA which subsequently integrated into the tumor genome. Analysis of M musculus subsp molossinus DNA revealed similar but shifted populations of A-particle genes, when compared with BALB/c DNA, except for the absence of a prominent EcoRI-HindIII band at 3.9 kilobases. This latter band, representing approx 15% of the A-particle genes in BALB/c DNA, was shown to be a deletion variant of the most abundant gene family. (Author abstract) (37 Refs)

63. LOSS OF THE SHORT LIVED SUPPRESSIVE FUNCTION OF PERIPHERAL LEUKOCYTES IN FELINE RETROVIRUS-INFECTED CATS (MEETING ABSTRACT)

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Proc Am Assoc Cancer Res; 23:1097 1982

This research examined the short-lived suppressive function of normal and retrovirus-infected (FeLV, feline leukemia virus) cat peripheral blood mononuclear cells (PBMC). Normal specific-pathogen-free cats (SPF) demonstrated an increased lymphocyte blast transformation (LBT) with a suboptimal amount of concanavalin A (con A, 0.1 ug/10(5) PBMC) after a 24 hour delay in mitogen addition as compared to 0 hour mitogenesis. The suppressive removal index (SRI) was calculated by a delta 24 hour mitogenesis /delta 0 hour mitogenesis. Increased stimulation after 24 hours which was not due to enhancing factors accumulating in the culture medium has been attributed to a short-lived suppressor cell function. The average SRI for normal SPF cats was 3.8. This phenomenon was subsequently studied in retrovirus-infected (FeLV) cats who demonstrated a loss of this function with an average SRI of 1.1 which was significantly lower than uninfected animals. This lower index was a result of a higher 0 hour mitogenesis. Therefore, this data suggests a loss of suppressor function during the viremic stages of feline leukemia which may be due to an overall immunosuppression of cellular immune functions including suppressor cells. Ultimately loss of suppressor cells may contribute to the findings of a Coomb's positive anemia associated with feline leukemia pathogenesis. (no Refs)

64. IN VITRO TRANSFORMATION BY AVIAN ERYTHROBLASTOSIS VIRUS RECRUITS CELLS OF ERYTHROID LINEAGE WITH VARYING DEGREE OF DIFFERENTIATION.

Therwath A, Scherrer K
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Int J Cancer; 29(5):555-558 1982

We have previously shown that the AEV infection of leukosis-free chickens provokes an erythroleukemia in the infected birds, and that the target cell for virus transformation is most likely an early pro-erythroblast comparable to the BFU-E. The virus infection correlates with a block in differentiation which was studied at a specific cellular gene level, namely that of the globin genes. In live birds, the viral transformation has been found to affect the transcriptional activity of two out of three

adult globin genes and the phenotypic expression of the third. Indeed, the alphaa gene that is transcribed is silent as well, since its transcription product is fully eliminated in the nucleus following an 'abortive processing'. Chick bone marrow cells can also be transformed in vitro by AEV in which case the virus recruits, as targets, cells of the erythroid lineage belonging to a wider spectrum and hence in varying degrees of differentiation. In contrast to the results obtained with in vivo transformed cells, molecular hybridization with globin cDNA probes showed that in the erythroblasts transformed in vitro under tissue culture conditions all the three adult globin genes are transcriptionally active. Judging from our present results, we may propose that AEV transformation in vitro does not shut off but only modulates the already functioning erythroid cell differentiation program. (14 Refs)

65. AVIAN LYMPHOID LEUKOSIS VIRUS INFECTION AND DNA INTEGRATION IN THE PRELEUKOTIC BURSAL TISSUES: A COMPARATIVE STUDY OF SUSCEPTIBLE AND RESISTANT LINES.

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Virology; 119(2):411-421 1982

Lymphoid leukosis (LL) is a naturally occurring neoplastic disease of chickens, caused by avian lymphoid leukosis virus (ALV). Most inbred lines of chickens, susceptible to virus infection, are also susceptible to LL development. An interesting exception is line 6(3) which rarely develops LL after virus infection. To obtain more information concerning the resistance of line 6(3) to LL, we have compared virus infection and integration in bursal tissues of resistant line 6(3) and a susceptible cross (15I(5) x 7(1)) after virus inoculation into day-old chicks. We report here that (a) the bursa tissues in both lines are infected to similar extent and (b) the initial viral infections in both lines lead to 'random' integration of proviruses in the chromosomes of the bursal tissues. Only in the tumors developing later in the susceptible line can specific integration of provirus near a cellular oncogene, c-myc, be detected. Based on these data, the mechanism of resistance of line 6(3) to LL is discussed. (Author abstract) (26 Refs)

66. IDENTIFICATION AND CHARACTERIZATION OF A TUMOR-SPECIFIC ANTIGEN EXPRESSED BY RETICULOENDOTHELIOSIS VIRUS-TRANSFORMED HEMATOPOIETIC CELLS (MEETING ABSTRACT)

Walker MH, Neisel DW, Bose HR
Microbiology Department, University of Texas, Austin, TX, 78712
Fed Proc; 41(3):897 1982

Birds infected with avian reticuloendotheliosis virus (REV-T) develop a fatal, acute lymphocytic leukemia within 7 to 14 days. The target cell for this replication-defective acute leukemia virus has been characterized as an immature lymphocyte expressing some B-cell determinants. Using 125I/hydrogen peroxide/lactoperoxidase cell-surface labelling and radioimmunoprecipitation with antiviral antisera, we have identified a polypeptide of 120,000 daltons (p120) that is expressed by each of 17 independently-derived clones of REV-T transformed lymphocytes. Furthermore, all clones of REV-T transformed nonvirus-producing lymphocytes which have been isolated do not synthesize detectable levels of viral structural polypeptides but do express p120. Therefore, we have characterized the structural relationship between p120 expressed by nonvirus-producing REV-T transformed clones and the viral envelope, major core and gag-pol precursor polypeptides by thin-layer peptide mapping. (no Refs)

67. ORGANOTROPISM OF THE LYMPHOPROLIFERATIVE DISEASE VIRUS (LPDV) OF TURKEYS.

Gazit A, Schwarzbard Z, Yaniv A, Ianconescu M, Perk K, Zimber A
Dept. Human Microbiology, Sackler Sch. Medicine, Tel-Aviv Univ., Tel-Aviv, Israel
Int J Cancer; 29(5):599-606 1982

Turkey poults were inoculated with lymphoproliferative disease virus (LPDV) of turkey, and the organotropism of the inoculated virus was determined from the kinetics of virus expression and tumor formation. Molecular hybridization experiments, conducted to determine the level of viral RNA expression in the various organs of infected birds, established lymphoid tissues, including bone marrow, as the target for LPDV infection. Of these, bone marrow was the first to be infected but subsequently virus replication extended to the thymus, the spleen and the bursa of Fabricius. The low level of LPDV expression in non-target organs probably stemmed from infiltration of infected lymphatic cells. The fact that the main organs for virus replication were not invariably the ones most clinically involved suggests that the target cells for virus infection need not necessarily be the targets for virus oncogenicity. A possible mode for LPDV infection and transformation is proposed. (Author abstract) (23 Refs)

REVIEWS AND OTHER RELATED STUDIES

68. GENETIC INFLUENCES IN HUMAN TUMORS.

Knudson AG
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Cancer - A Comprehensive Treatise Vol. 1. Etiology - Chemical and Physical Carcinogenesis. Second Edition. Becker FF, ed. New York, Plenum Press, 714 pp., 1982.

Genetic states predisposing to cancer include chromosomal disorders such as Down's syndrome and Klinefelter's syndrome with increased risks of leukemia. The syndromes of Fanconi and Bloom are both autosomal recessive disorders which predispose to leukemia and cancer. Ataxia-telangiectasia is another autosomal recessive disease associated with chromosomal abnormality and a strong predisposition to lymphoid neoplasia. Xeroderma pigmentosum is a genetic state which predisposes to environmentally induced skin cancer. Dominantly inherited tumors differ sharply from the genetic conditions previously discussed in that tumor is a critical phenotypic feature and occurs with high penetrance. In some instances, a tumor is part of a syndrome, other manifestations of which are other kinds of tumors or nonneoplastic signs. In other instances tumor occurs in just one tissue, although it may be multiple in that tissue. Tumor syndromes include polyposis of the colon, Gardner's syndrome, hereditary adenocarcinomatosis, basal cell nevus syndrome, multiple endocrine tumor syndromes, neurofibromatosis, von Hippel-Lindau syndrome and tuberous sclerosis. Specific tumors which are inherited but not part of a syndrome are retinoblastoma, Wilms' tumor of the kidney and neuroblastoma. (57 Refs)

69. CYTOGENETICS.

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Dept. Pathology, Sch. Medicine, Univ. Pennsylvania, Philadelphia, PA
Cancer - A Comprehensive Treatise Vol. 1. Etiology - Chemical and Physical Carcinogenesis. Second Edition. Becker FF, ed. New York, Plenum Press, 714 pp., 1982.

Present knowledge in the field of chromosome alterations in tumor cells is reviewed and the significance of certain findings is discussed. Human leukemias have been more extensively studied cytogenetically than any other group of tumors and have provided much of the data upon which three generalizations about malignancy and cytogenetics are based. These general statements based on leukemia research are that most tumors are chromosomally abnormal, that chromosome alterations are often the same in all cells of a given tumor, and that neoplasms of a particular type do not show a consistent cytogenetic alteration from one tumor to another. A specific change occurring in nearly every tumor of a given type, such as the Philadelphia chromosome in human chronic granulocytic leukemia is the exception, rather than the rule. Nearly all human malignant solid tumors studied to date have shown chromosome abnormalities with only a few cases reported in which the karyotype appeared normal. In addition to human leukemias and solid tumors, other areas reviewed are chromosome breakage and cancer, cytogenetics of cells in culture, animal tumors, and a discussion of chromosome changes and tumor initiation and progression. The clinical applications of tumor chromosome studies include the diagnostic use of chromosome data to aid in the classification of confusing cases of human leukemia. (206 Refs)

70. THE EPSTEIN-BARR VIRUS: HISTORICAL, BIOLOGIC, PATHOLOGIC AND ONCOLOGIC CONSIDERATIONS.

Seemayer TA, Oligny LL, Gartner JG
Dept. Pathology, Montreal Children's Hosp., Montreal, Quebec, Canada
Perspect Pediatr Pathol; 6:1-33 1981

The biological nature of Epstein-Barr virus (EBV) and clinical manifestations of human EBV infection and of several related disorders (infectious mononucleosis, fatal infectious mononucleosis, X-linked lymphoproliferative syndrome, Burkitt's lymphoma, nasopharyngeal carcinoma, ataxia-telangiectasia, cytomegalovirus) are reviewed. Immunoblastic sarcoma of B lymphocytes is discussed, and mechanisms to account for the failure of human immune defenses against EBV and subsequent development of carcinoma are proposed. (168 Refs)

71. SURFACE GLYCOPROTEINS OF MALIGNANT HUMAN LEUKOCYTES.

Gahmberg CG, Andersson LC
Dept. Biochemistry, Univ. Helsinki, Helsinki, Finland
Biochim Biophys Acta; 651(2/3):65-83 1982

The biochemistry of cell surface glycoproteins of malignant WBC is reviewed. Topics discussed include surface glycoproteins of normal hematopoietic cells, cultured cell lines for malignant WBC (Epstein-Barr virus positive and negative lymphoma cell lines, histiocytic lymphoma lines, T cell leukemia, non-T, non-B cell leukemia, hairy cell leukemia, erythroleukemic cell line K562, the HL-60 promyelocytic cell line), and surface glycoproteins from patients with leukemias and lymphomas. (138 Refs)

72. OTHER LEUKEMIAS AND RELATED DISEASES: ON HEMOPOIETIC DYSPLASIA AND CHRONIC MYELOPROLIFERATIVE DISORDERS.

Sawada H, Yamagishi H, Uchino H
First Dept. Internal Medicine, Kyoto Univ. Sch. Medicine, Kyoto, Japan
Nippon Rinsho; 39(8):2749-2755 1981

Preleukemic state is characterized by specific blood abnormalities prior to the clinical confirmation of leukemia. Prospectively, hematological abnormality similar to preleukemia state will not be a necessary condition for transformation into leukemia. Hemopoietic dysplasia (HD) is defined as a panmyelopathy presenting abnormality in all three lines of hematopoietic cells, and leads eventually to leukemia. HD should not be confused with the myelodysplastic syndrome at this time. Erythroleukemia mainly shows abnormal formation of erythrocytic hematopoietic tissue and of other cell lines, such as granulocytic cells. Refractory anemia with excess of myeloblasts (RAEM) is found more in 60-70-yr-old people, and morphologically shows abnormality in the three myelocytic cell lines. Chronic myelomonocytic leukemia is similar to RAEM but no increase of monocytic immature cells is seen. Idiopathic myelofibrosis is characterized by osteosclerosis accompanied by extramedullary hematopoiesis. Polycythemia vera shows an increase in the peripheral erythrocytes and in the blood volume. Primary thrombocythemia differs from chronic myelocytic leukemia in the negative Philadelphia chromosome and in the high NAP. Acute myelofibrosis shows increase in megakaryocytes and megakaryoblasts without splenomegaly. Relationship among the above disorders is discussed. (28 Refs) (In JPN)

73. ENVIRONMENTAL FACTORS AND MALIGNANT HEMATOLOGICAL DISEASES.

Bjorkholm M
Hemataologsektionen, Danderyds sjukhus, Danderyd, Sweden
Lakartidningen; 79(15):1457-1459 1982

Environmental factors and their possible or demonstrated etiological role in malignant hematological diseases are reviewed. Ionizing radiation is a well-established cause of leukemia, but no relationship between exposure to such radiation and chronic lymphocytic leukemia was found. Benzene is considered as a leukemogenic factor, even though it was not possible to induce leukemia with benzene in experimental animals. Environmental factors during childhood may play a role in the development of Hodgkin's disease. (44 Refs) (In SWE)

74. SIGNIFICANCE OF ENVIRONMENTAL FACTORS FOR THE DEVELOPMENT OF LEUKEMIA, MYELOMA AND MALIGNANT LYMPHOMA.

Brandt L
Onkologiska kliniken, Lasarettet, Lund, Sweden
Lakartidningen; 79(15):1490-1492 1982

Studies on environmental factors in the etiology of leukemias, myelomas and lymphomas are reviewed. Ionizing radiation plays a role in the development of acute myeloid leukemia, acute lymphocytic leukemia, chronic myeloid leukemia, myeloma, Hodgkin's disease and non-Hodgkin's lymphomas, but probably none in chronic lymphocytic leukemia. Viral etiology of chronic lymphocytic leukemia in farm workers and of Burkitt's lymphoma and of other non-Hodgkin's lymphomas is suspected. Hodgkin's disease was found to be overrepresented among men exposed to chemicals. (35 Refs) (In SWE)

75. SCIENTIFIC STRATEGIES TO SAVE YOUR LIFE.

Bross ID
Roswell Park Memorial Inst. Cancer Research, Buffalo, NY
Scientific Strategies to Save Your Life. New York, Marcel Dekker, Inc., Statistics-Textbooks and Monographs, Vol. 35, 259 pp., 1981.

The public health problems associated with hazardous technological products and processes are discussed, with emphasis on the risks of low-level radiation exposure. Data presented to the Nuclear Regulatory Commission based on results of the Tri-State Survey carried out in areas of upstate New York, Maryland, and Minnesota are considered. Analysis of the incidence of leukemia and indicator diseases in a population base of 13 million persons has shown that the children of persons exposed to low-level radiation have a relative risk of 50 for leukemia and a relative risk of 5 for the indicator childhood disease (asthma, eczema, urticaria, pneumonia, dysentery, or rheumatic fever). Both the linear extrapolation model and the threshold model fail to fit the observed disease counts. These findings are interpreted as an indication that the actual dose-response curve flattens as it approaches the 1-rad range and the extrapolative estimates seriously underestimate the actual risk of the low-level radiation. Public health issues involved in the controversy over low-level radiation include the specification of permissible exposure levels in the nuclear industry and cost-benefit analysis of mass screening programs for breast cancer. A cost-to-benefit ratio of 125:1 is thought to be based on a miscalculation. Propagation of such an error may lead to a serious underestimation of the risk of mammography in women less than 50 yr old. (53 Refs)

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NOTICE OF CURRENT REVIEWS: CARCINOGENESIS

As an additional service to readers of carcinogenesis (CK series) CANCERGRAMS, each issue now provides a bibliography of review articles of interest to carcinogenesis researchers, selected from journals screened for that month's CANCERGRAMS.

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1. MICROWAVE HEATING ENHANCES THE MIGRATION OF PLASTICIZERS OUT OF PLASTICS.
Bishop CS, Dye A
East Tennessee State Univ., Johnson City, TN, 37614
J Environ Health; 44(5):231-235 1982

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Konietzko H, Fischer G
Institut fur Arbeits- und Sozialmedizin, Johannes-Gutenberg-Universitat, Obere Zahlbacher Strasse 67, D-6500 Mainz, W. Germany
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3. NITROSAMINES.
Aigner K
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Wien Med Wochenschr; 132(71,Suppl):75-79 1982
In GER

4. EXPERIMENTAL TUMORS OF THE PERIPHERAL NERVOUS SYSTEM.
Beniashvili DS
Cancer Res. Center, Tbilisi, USSR
Eksp Onkol; 4(2):12-19 1982
In RUS

5. MUTAGENIC, CARCINOGENIC AND TERATOGENIC EFFECTS OF STYRENE.
Sram RJ, Pohlova H, Topinkova E
Klinika hygieny a epidemiologie, Srobarova 48, 100 42 Prague 10, Czechoslovakia
Prac Lek; 34(2):68-72 1982
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6. DIETHYLSTILBESTROL: EFFECT OF IN UTERO EXPOSURE.
Burke L
Obstetrics/Gynecology Dept., Harvard Medical Sch., Boston, MA
Curr Probl Obstet Gynecol; 5(2):1-58 1981

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Stillman RJ
Dept. Obstetrics and Gynecology, George Washington Univ. Sch. Medicine and Health Sciences, 2150 Pennsylvania Ave., NW, Washington, DC, 20037
Am J Obstet Gynecol; 142(7):905-921 1982

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Petersen R, Ehrhorn H, Mousing K, Sabroe S, Silberschmid M, Venstrup-Nielsen SE
Socialmedicinsk institut, Vesterbro Torv 1-3, DK-8000 Arhus C, Denmark
Ugeskr Laeger; 144(13):971-975 1982
In DAN

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9. NATURALLY OCCURRING FOOD TOXICANTS: PHENOLIC SUBSTANCES OF PLANT ORIGIN COMMON IN FOODS.
Singleton VL
Dept. Viticulture and Enology, Univ. California, Davis, CA
Adv Food Res; 27:149-242 1981

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Sugimura T
Natl. Cancer Res. Inst., Tsukiji, Chuo-ku, Tokyo, Japan
Cancer; 49(10):1970-1984 1982

11. THE BIOLOGICAL EFFECTS OF CARRAGEENAN AND OTHER SULFATED POLYSACCHARIDES WITH PARTICULAR ATTENTION TO IMMUNOLOGICAL AND CARCINOGENIC PROPERTIES.
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Sivak A, Rudenko L, Teague LG
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Prev Med; 11(2):232-239 1982

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15. STUDIES OF CANCER EPIDEMIOLOGY IN THE UNITED STATES OF AMERICA.
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16. CURRENT CONCEPTS OF THE ETIOLOGY AND PATHOGENESIS OF LUNG CANCER.
Chaklin AV, Gritsiute LA
No affiliation given
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17. ETIOLOGY OF MOUTH AND LIP TUMORS.
Zaberzhinskii MA, Godorozha PD
N. N. Petrov Res. Inst. Oncology, Leningrad, USSR
Vopr Onkol; 28(2):105-113 1982
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18. PSYCHIATRIC ASPECTS OF CANCER.
Peterson LG, Popkin MK, Hall RC
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Omenn GS
Dept. Environmental Health, Univ. Washington, Seattle, WA, 98195
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21. POLYCHLORINATED BIPHENYLS (PCBS): AN AUSTRALIAN VIEWPOINT ON A GLOBAL PROBLEM.
Richardson BJ, Waid JS
Marine Science Lab., Ministry for Conservation - Victoria, P.O. Box 114, Queenscliff, Victoria 3225, Australia
Search; 13(1/2):17-25 1982

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Lakartidningen; 79(15):1490-1492 1982
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23. ENVIRONMENTAL FACTORS AND MALIGNANT HEMATOLOGICAL DISEASES.
Bjorkholm M
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Lakartidningen; 79(15):1457-1459 1982
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CELLULAR AND MOLECULAR MECHANISMS IN CARCINOGENESIS

24. REGULATION OF GENE EXPRESSION IN NORMAL AND NEOPLASTIC CELLS. A REVIEW.
Hochhauser SJ, Stein GS, Stein JL
Dept. Biochemistry and Molecular Biology, Univ. Florida, Coll. Medicine, Gainsville, FL, 32610
Pathobiol Annu; 11:1-29 1981

25. WHAT ARE ISOZYMES TELLING US ABOUT GENE REGULATION IN CANCER?
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Nishino H, Inui K
Dept. Biochemistry, Kyoto Prefectural Medical Univ., Kyoto, Japan
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27. CURRENT VIEWS ON THE NATURE OF MYOEPITHELIAL CELLS AND THEIR ROLE IN THE MORPHOGENESIS OF DYSHORMONAL HYPERPLASIAS AND BREAST TUMORS.
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Central Lab. Pathology, Inst. Human Morphology, Moscow, USSR
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28. OVERVIEW: RETINOIDS AND CARCINOGENESIS.
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Dept. Veterinary Science, Coll. Agricultural and Life Sciences, Univ. Wisconsin, 1655 Linden Drive, Madison, WI, 53706
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Komarova EA, Kriukova IN
All-Union Cancer Res. Center, Moscow, USSR
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Rowe WP
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Cancer; 49(10):1958-1962 1982

33. THE PERSISTENCE OF RETROVIRUSES.
Weiss RA
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Symp Soc Gen Microbiol; 33:267-288 1982

34. HOW DO PAPOVA VIRUSES PERSIST IN THEIR HOSTS?
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Symp Soc Gen Microbiol; 33:227-247 1982

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Groopman JE, Gottlieb MS
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Hosp Pract; 17(5):64F-64G,64J,64N,64O,64R,64T 1982

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37. MAJOR APPROACHES TO THE EXPERIMENTAL STUDY OF LUNG CANCER.
Plisa GB, Turusov VS, Zabezhinskii MA
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Watson JD
Cold Spring Harbor Lab., Box 100, Cold Spring Harbor, NY, 11724
Cold Spring Harbor Symp Quant Biol 45(part 1): 445 pp., 1981.

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ORGAN SITE CARCINOGENESIS

Lymphatic and Hematopoietic Tissues

SERIES CK20 No. 82/11 NOVEMBER, 1982

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EPIDEMIOLOGY AND ETIOLOGY OF HUMAN LYMPHORETICULAR MALIGNANCIES: VIRAL STUDIES

1. BURKITT-TYPE LYMPHOMA IN FRANCE AMONG NON-HODGKIN MALIGNANT LYMPHOMAS IN CAUCASIAN CHILDREN.

Philip T, Lenoir GM, Bryon PA, Gerard-Marchant R, Souillet G, Philippe N, Freycon F, Brunat-Mentigny M
Paediatric Oncology Unit, Centre Leon-Berard, 28, rue Laennec, 69273 Lyon cedex 2, France
Br J Cancer; 45(5):670-678 1982

In a retrospective analysis of 87 cases of Caucasian childhood non-Hodgkin malignant lymphoma (NHML) from Lyon, France, all the cases were diffuse lymphomas, but 47 were diagnosed as monomorphic small non-cleaved NHML, patho-

HE 20.3173/2:

logically indistinguishable from Burkitt's lymphoma (BL). BL could then be the most frequent childhood lymphoma in France. This homogeneous series allows better definition of the characteristics of BL within NHML. Age distribution is similar to that of endemic BL, with a sex ratio of 3.7/1. Abdominal masses are initially present in 68% of the cases, whereas jaw is involved in only 4%. The disease is characterized by its overwhelming evolution in the absence of therapy. However, complete remission (CR) is usually obtained after the first chemotherapy regimen. Most relapses occur at 3-8 mo. Death could be related to cerebrospinal fluid (CSF) involvement, local recurrence or secondary marrow involvement. Ninety percent of the patients alive with no evidence of disease (NED) 8 mo after CR can be considered as definitely cured. Our study on Caucasian children with NHML indicates that, from histological and clinical criteria, nearly half the cases are very similar to African BL. Even though EBV rarely associated with our cases, BL could be a worldwide lymphoma. (Author abstract) (41 Refs)

2. THE FIRST REAL HUMAN TYPE-C RETROVIRUS.

Epstein MA

Dept. Pathology, Univ. Bristol, Bristol BS8 ITD, England

Immunol Today; 3(3):61-62 1982

Recent advances with respect to the human T leukemia virus (HTLV) are reviewed. HTLV may eventually be proven the etiological agent in adult T cell leukemia, thus adding HTLV to the known association of Epstein-Barr virus with Burkitt's lymphoma and nasopharyngeal carcinoma and hepatitis B virus with primary hepatocellular carcinoma. Human oncogenic viruses may be responsible for a very significant proportion of human malignant disease worldwide. (7 Refs)

3. ANTIBODIES TO ADULT T-CELL LEUKEMIA-VIRUS-ASSOCIATED ANTIGEN (ATLA) IN SERA FROM PATIENTS WITH ATL AND CONTROLS IN JAPAN: A NATION-WIDE SERO-EPIDEMIOLOGIC STUDY.

Hinuma Y, Komoda H, Chosa T, Kondo T, Kohakura M, Takenaka T, Kikuchi M, Ichimaru M, Yunoki K, Sato I, Matsuo R, Takiuchi Y, Uchino H, Hanaoka M

Inst. Virus Res., Kyoto Univ., Kyoto 606, Japan

Int J Cancer; 29(6):631-635 1982

A nation-wide sero-epidemiologic survey of adult T-cell leukemia virus (ATLV), detected as anti-ATLA (ATLV-associated antigen), was made in Japan. Sera from adult donors in 15 different locations were screened for anti-ATLA. High incidences (6 to 37%) of antibody-positive donors were found in seven regions, one in northern Japan, and the others in southwestern regions. These areas are ATLV-endemic areas corresponding to ATL-endemic areas. Examination of sera from healthy donors aged 6 to 80 yr in ATL-endemic areas showed an age-dependent increase of seropositive donors with a maximum of about 30% to 40 yr of age. Anti-ATLA was found in all but two of 142 patients with ATL. Anti-ATLA-positive patients with ATL were mainly found in ATLV-endemic areas and only a few in ATL-nonendemic areas. Six patients with cutaneous T-cell lymphoma in ATLV-nonendemic areas gave a negative reaction for anti-ATLA. The geometric mean titer of anti-ATLA of patients with ATL was higher than that of healthy donors. (Author abstract) (9 Refs)

EPIDEMIOLOGY AND ETIOLOGY OF HUMAN LYMPHORETICULAR MALIGNANCIES: OTHER STUDIES

4. FAMILIAL T-CELL LYMPHOBLASTIC LYMPHOMA: ASSOCIATION WITH VON RECKLINGHAUSEN NEUROFIBROMATOSIS AND GARDNER SYNDROME.

Kaplan J, Cushing B, Chang CH, Poland R, Roscamp J, Perrin E, Bhaya N

Children's Hosp. Michigan, 3901 Beaubien Blvd., Detroit, MI, 48201

Am J Hematol; 12(3):247-250 1982

A family is described in which three of seven siblings developed a T-cell lymphoblastic lymphoma. Tumor cells formed rosettes with sheep erythrocytes, lacked surface Ig, and expressed human T- but not B-lymphocyte antigens. They lacked the enzyme terminal transferase suggesting a lymph node rather than thymic T-cell origin. Autopsy findings supported this conclusion. All three sibs, like their father, had numerous cafe au lait spots indicative of Von Recklinghausen neurofibromatosis. One child had a sc fibroma, and another had multiple colonic polyps and exostoses characteristic of Gardner syndrome. Both are autosomal dominant conditions known to predispose to malignancies. The genetic factors responsible for these conditions may also predispose to the development of 'post-thymic' T-cell lymphoblastic lymphoma. (Author abstract) (10 Refs)

EPIDEMIOLOGY AND ETIOLOGY OF NON-HUMAN LEUKEMIA AND LYMPHOMA

5. CAUSES OF DEATH AND SEX DIFFERENCES IN SURVIVAL TIMES OF PIGS WITH UNTREATED HEREDITARY LYMPHOSARCOMA (LEUKEMIA).

McTaggart HS, Imlah P, Head KW

Royal (Dick) Sch. Veterinary Studies, Univ. Edinburgh, Edinburgh, Scotland

JNCI; 68(2):239-248 1982

The survival times from birth of 39 entire male Large White pigs with hereditary lymphosarcoma (L/S) were significantly shorter than those of 76 affected females. The survival times of 19 male castrates were for the most part intermediate between those for entire males and females. Analysis of the cause of death revealed that pigs with L/S (L/S-P) were more likely than pigs without L/S to die from colibacillosis, but this disease showed no sex predisposition. In uncomplicated deaths from L/S, weights of splanchnic lymph nodes, spleen, and thymus were greatest in females. The cell-mediated and humoral antibody responses of L/S-P were significantly poorer against 2,4-dinitrofluorobenzene (DNFB) and sheep red blood cells, poorer against skin homografts, but better against bovine serum albumin than those of healthy littermates. Healthy females had stronger DNFB reactions than did healthy males or castrates. Castrated L/S-P responded to DNFB better than did females and significantly better than did entire males. (Author abstract) (28 Refs)

6. ILEOCECAL (PARACECAL) MALIGNANT LYMPHOMA--IMMUNOBLASTOMA--IN HOODED RATS.

Nemeth P, Schneider J, Warzok R
Korbontani Intezet, POTE, Szigeti u. 12, 7643 Pecs, Hungary
Morphol Igazsagugyi Orv Sz; 22(2):117-123 1982

Spontaneous and chemically induced ileocecal (paracecal) malignant lymphoma (immunoblastoma) was studied in inbred strain E hooded rats compared with untreated outbred Wistar rats. The spontaneous incidence of ileocecal immunoblastoma was found to be 5% in 95 untreated hooded rats, and the tumors were detected between days 545 and 740 of life. The spontaneous incidence was found to be 0% among more than 400 untreated Wistar rats of two different strains. The immunoblastoma incidence was found to be 8-41% among hooded rats treated prenatally or postnatally with the combinations of ethylurea (0.5%), methylurea (0.2-0.3%), isopropylurea (0.4%), n-propylurea (0.4%), butylurea (0.4%) in drinking water or ephedrine (0.5% in feed) or Obesin (40 mg/kg with 0.2-0.5% sodium nitrite in feed or 40 mg/kg 12 times every 2 wk through gastric probe). The incidence was found to be highest in the group treated with the combination of 0.4% propylurea and 0.3% sodium nitrite postnatally and lowest in that treated with 0.4% isopropylurea and 0.3% sodium nitrite postnatally. The tumors were detected in the treated animals between days 194 and 789 of life. The induced tumors were identified histologically as transfollicular immunoblastomas, showing no difference from the spontaneous ones. The tumor incidence was increased and the latent period shortened by treatment with the N-nitroso compounds. (22 Refs) (In HUN)

CYTOGENETIC AND MORPHOLOGIC STUDIES

7. THE PROGNOSTIC VALUE OF CHROMOSOME STUDIES IN PATIENTS WITH THE PRELEUKEMIC SYNDROME (HEMOPOIETIC DYSPLASIA).

Anderson RL, Bagby GC
Medical Res., Veterans Admin. Medical Center, Portland, OR, 97201
Leuk Res; 6(2):175-181 1982

Influence of chromosome abnormalities (CAB) in bone marrow cells in preleukemic patients on disease progress was investigated and the independent effect of prior alkylating agent exposure on prognosis was analyzed. Clonal abnormalities were observed in 15 of the 42 patients included into the study. CAB were observed in patients with known prior alkylating agent exposure. Eight patients with evaluable cytogenetic studies had received prior alkylating agent chemotherapy for underlying malignant or rheumatic diseases. Acute leukemia developed more frequently in this group (7/8) than among alkylator-unexposed patients (8/34). The group of nine patients with complex CAB were also significantly more likely to develop leukemia than were patients with normal chromosomes. The two poor prognostic groups overlapped significantly so that the relative importance of prior alkylating agent exposure and complex cytogenetic rearrangements could not be assessed. Trends towards poorer leukemia-free survival were observed among patients with only abnormal metaphases and poorer overall survival among both alkylating agent exposed patients and patients with complex cytogenetic rearrangements but statistical significance has not been reached. Results indicated that the presence of simple cytogenetic abnormalities does not necessarily predict early leukemic evolution. (21 Refs)

8. FURTHER CYTOGENETIC STUDIES ON ACUTE PROMYELOCYTIC LEUKEMIA.

Kondo K, Sasaki M
(c/o Sasaki) Chromosome Res. Unit, Hokkaido Univ., Sapporo 060, Japan
Cancer Genet Cytogenet; 6(1):39-46 1982

Chromosomes were analyzed in nine cases of acute promyelocytic leukemia (APL-M3), including a follow-up case and an erroneously diagnosed case from our previous reports. The reciprocal 15; 17 translocation, t(15q+; 17q-), was found in all cases, and the break points were estimated to be 15q22 or q23 and 17q12. In addition, trisomy 8 and an isochromosome of the long arm of the affected chromosome number 17, i(17q-), were observed in two cases each. Some other abnormalities were encountered, mostly in remission or relapse. The disappearance and repopulation of t(15q+; 17q-) cells were associated with complete remission and relapse, respectively, in two repeatedly analyzed cases. Including the previously reported cases, we investigated a total of 12 cases of APL, and all were found to be associated with t(15q; 17q-). The mean age of the 12 patients was 34.25 +-3.12 (SD) yr, and their mean survival 266.3 +-95.67 (SD) days. (Author abstract) (22 Refs)

9. FURTHER CHARACTERIZATION OF ACUTE MYELOGENOUS LEUKEMIA WITH T(8; 21) CHROMOSOME TRANSLOCATION.

Sakurai M, Kaneko Y, Abe R
Saitama Cancer Center, 818 Komuro, Ina, Saitama 362, Japan
Cancer Genet Cytogenet; 6(2):143-152 1982

All seven patients with t(8; 21)(q22; q22) and one with a del(8)(q22) had a diagnosis of acute myelogenous leukemia (AML)-M2 type. Similar morphologies of leukemic cells with a t(8q-; 21q+) or with an 8q-, as well as the association of the latter with loss of a sex chromosome, indicated that the translocation or deletion of chromosome No 8 at q22 may be essential to the phenotypic expression and loss of a sex chromosome in cells with the translocation. Seven patients (1 in Group I, 4 in Group II, and 2 in Group III) were in remission and four relapsed. All patients at relapse had acquired additional autosomal abnormalities, which were related to changes in cell morphology and relapse. (Author abstract) (29 Refs)

10. KARYOTYPE ANALYSIS IN ACUTE NONLYMPHOCYTIC LEUKEMIA (ANLL): COMPARISON WITH ETHNIC GROUP, AGE, MORPHOLOGY, AND SURVIVAL.

Bernstein R, Pinto MR, Morcom G, Macdougall LG, Bezwoda W, Dukes I, Penfold G, Mendelow B
Dept. Human Genetics, S.A.I.M.R., P.O. Box 1038, Johannesburg 2000, South Africa
Cancer Genet Cytogenet; 6(3):187-199 1982

The karyotype leukemic cell morphology (FAB classification), ethnic group, age, sex, and survival were compared in 60 patients with acute nonlymphocytic leukemia (ANLL) to determine their diagnostic and prognostic significance. An ethnic age difference was observed; a significantly greater number of black patients were children. The majority of children were males. A higher frequency of chromosome abnormalities was detected in children, yet they survived longer than adults. A specific, significant association between a t(8;21) karyotype and M2-ANLL was confirmed; 4 of 10 patients with M2-ANLL showed this translocation. The more mature morphology of M2-ANLL was associated with a longer survival irrespective of karyotype, ethnic group, and age. The specificity of t(15;17)

in M3-ANLL and nonrandom monostomy 7 in preleukemic children was confirmed. Patients, particularly adults, with normal karyotypes tended to survive longer than those with abnormal karyotypes. The patient's age and the differentiative capacity of the leukemic cell appear to be as important as the karyotype in determining survival. The nonrandom association of certain chromosome aberrations in ANLL appears to be worldwide. (Author abstract) (32 Refs)

11. PH1-POSITIVE CML ASSOCIATED WITH MEGAKARYOCYTIC HYPERPLASIA AND THROMBOCYTHEMIA AND AN ABNORMALITY OF CHROMOSOME NO. 3.

Carbonell F, Hoelzer D, Thiel E, Bartl R
Abteilung fur klinische Physiologie und Arbeitsmedizin, Universitat Ulm, Oberer Eselsberg M24, D-7900 Ulm, W. Germany
Cancer Genet Cytogenet; 6(2):153-161 1982

A patient with Philadelphia (Ph1) chromosome positive chronic myelocytic leukemia is described, who had in blast crisis in addition to an abnormality of chromosome No 3; ins(3; 3)(q26; q21q26). This abnormality might be connected with hyperplasia of megakaryocytes and thrombocythemia, as recently reported in patients with acute leukemia. In the initial phase of the disease our patient had also thrombocythemia, hyperplasia of megakaryocytes with morphological abnormalities. Furthermore, when blast cells were cultured in diffusion chambers, differentiation into several cell lines occurred but not into megakaryopoiesis. It is, therefore, concluded that the involved band on chromosome No 3 might contain the locus which controls megakaryocytic proliferation and platelet production but additional factors seem to be required for their expression. (Author abstract) (19 Refs)

12. CLONAL ORIGIN OF THE PHILADELPHIA TRANSLOCATION IN CHRONIC MYELOID LEUKEMIA DEMONSTRATED IN SOMATIC CELL HYBRIDS USING AN ADENYLATE KINASE-1 POLYMORPHISM.

Geurts van Kessel AH, Van Agthoven AJ, Hagemeijer A
Dept. Cell Biology and Genetics, Erasmus Univ., P.O. Box 1738, 3000 DR Rotterdam, The Netherlands
Cancer Genet Cytogenet; 6(1):55-58 1982

Hybrid cell lines were derived from fusion of rodent cells with leukocytes from a t(9q+; 22q-)-positive chronic myeloid leukemia (CML) patient carrying a chromosome No 9-linked adenylate kinase-1 (AK1) polymorphism (AK1 1-2). The AK1*2 allele was consistently expressed when 9q+ was present, whereas the AK1*1-coded isozyme was formed when the normal chromosome No 9 was present. These results provide additional data confirming the clonal origin of the Ph1 translocation in CML. (Author abstract) (13 Refs)

13. SISTER CHROMATID DIFFERENTIATION AND CELL-CYCLE-SPECIFIC PATTERNS IN CHRONIC MYELOCYTIC LEUKEMIA AND NORMAL BONE MARROW.

Becher R, Schmidt CG
Innere Universitatsklinik (Tumorforschung), D-4300 Essen 1, W. Germany
Int J Cancer; 29(6):617-620 1982

After in vitro incubation with bromodeoxyuridine (BrdUrd)-containing medium, metaphases of Philadelphia (Ph1)-chromosome positive cells in the blood and/or bone marrow of eight untreated patients with chronic myelocytic leukemia (CML) were analyzed by means of sister chromatid differentiation (SCD) and compared to 10 normal bone marrows. The majority of proliferating Ph1-positive cells (range: 46-86%) were unable to complete more than one cell cycle during the culture period of 50 hr (M1 metaphases). Ph1-positive M2 metaphases which had completed two cell cycles were found in the range of 18-54% and almost no M3 metaphases were detected after passage through three cell cycles (0-1%). The corresponding findings in proliferating normal bone-marrow cells were: M1 (13-68%), M2 (30-79%) and M3 (0-18%). These data support the notion that there is a prolonged cell cycle time in CML which can be measured by SCD, demonstrating a proportional shift from M3/M2 to M1 metaphases. SCD is suggested for kinetic studies on human malignant cell clones characterized by marker chromosomes. (Author abstract) (18 Refs)

14. SISTER CHROMATID EXCHANGE AND GROWTH KINETICS IN CHRONIC MYELOID LEUKEMIA.

Stoll C, Oberling F, Roth MP
Institut de Puericulture, Hopital Civil, 23, rue de la Porte de lHoptial, 67000 Strasbourg, France
Cancer Res; 42(8):3240-3243 1982

The frequency of sister chromatid exchange (SCE) was analyzed in bone marrow cells of 16 patients with chronic myeloid leukemia. We have compared the SCE frequency in these patients, in both chronic and blastic phases of the disease, to that of normal individuals. The frequency of SCE in blastic-phase chronic myeloid leukemia patients (mean, 1.86/cell) was significantly lower than that in chronic phase (mean, 2.96/cell), which was in turn lower than that in normal individuals (mean, 4.108/cell). We have used the SCE data to compare the rates of division of the bone marrow cells. Cells from chronic myeloid leukemia patients divided more slowly than did those from normal individuals, those from blastic-phase patients being slowest. (Author abstract) (31 Refs)

15. CHROMOSOME ABERRATIONS AND SISTER CHROMATID EXCHANGES IN CULTURED HUMAN LYMPHOCYTES TREATED WITH DIETHYLSTILBESTROL DIPROPIONATE.

Dzhangulashvili NA
Medical Inst., Tbilisi, USSR
Tsitol Genet; 16(2):24-29 1982

Mutagenic activity of diethylstilbestrol dipropionate (DES) at different concentrations was studied in cultured human peripheral blood lymphocytes. DES at 1.3 x 10(-6) M and 1.3 x 10(-5) M increased the incidences of aberrant metaphases (1.94% and 4.80%, respectively, compared with 0.49% after exposure of the cells to DES at 1.3 x 10(-7) M and 0.23% in untreated control cells). The incidences of sister chromatid exchanges after exposure of the cells to DES at 1.3 x 10(-6) M and 1.3 x 10(-5) M were 12.37% and 11.78%, respectively, compared with 7.17% after exposure of the cells to DES at 1.3 x 10(-7) M and 7.98% in untreated control cells. (33 Refs) (In RUS)

16. COMPARATIVE EFFICACY OF INDUCTION OF SISTER CHROMATID EXCHANGES BY ETHYLENE IMINE DERIVATIVES IN CULTURED HUMAN LYMPHOCYTES.

Listopad GG, Chebotarev AN
Inst. Medical Genetics, Moscow, USSR
Tsitol Genet; 16(2):34-38 1982

Mutagenic activities of six N-phosphoryl derivatives of ethylene imine (EI) were studied in cultures of human peripheral blood lymphocytes. The EI derivatives produced dose-dependent increases in incidences of sister chromatid exchange (SCE). Mutagenic activities of the polyfunctional EI derivatives were significantly greater than those of the monofunctional derivatives. The linear increase that was observed in the yield of SCE after exposure of the cultures to monofunctional derivatives indicated that the formation of cross-links was not a necessary requirement for SCE induction. (5 Refs) (In RUS)

17 SCE IN BLOOM SYNDROME B AND T LYMPHOCYTES.

Block AM, Shiraishi Y, Sandberg AA
(c/o Sandberg), Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
Clin Genet; 21(3):184-186 1982

Sister chromatid exchange (SCE) levels were studied in mixed lymphocyte populations from five patients with Bloom's disease. When cells were treated with mitogens that stimulated T and B cells, no significant differences in SCE were noted between the two populations. Gaps, ring chromosomes and quadriradials were noted; double minutes were noted in lipopolysaccharide-stimulated cultures in one patient. (7 Refs)

18. NORMAL SISTER CHROMATID EXCHANGE FREQUENCY IN LONG-TERM SURVIVORS WITH ACUTE LEUKEMIA.

Inoue S, Brown L, Ravindranath Y, Ottenbreit MJ
Children's Hosp. Michigan, Detroit, MI, 48201
Cancer Res; 42(7):2906-2908 1982

We hypothesized that the sister chromatid exchanges assay in acute leukemia long-term survivors may detect: (a) long-term effects of combined chemo- and radiotherapy; and possibly (b) those individuals with inherently deficient DNA repair. Accordingly, we determined the sister chromatid exchanges frequency in 26 blood specimens from 24 acute leukemia long-term survivors (patients) and 14 blood specimens from 13 control subjects (controls). The patients consisted of 23 children with acute lymphocytic and one child with acute myelocytic leukemia. The median length of chemotherapy was 5 years. Eighteen of the 24 patients also received prophylactic fractional central nervous system irradiation for the first 3 years of treatment, and one patient received therapeutic irradiation to the central nervous system. The median off-therapy period at the time of study was 2.5 years with a range of 0 to 7.5 years. The controls consisted of the parents of the patients and laboratory personnel. A mean exchange score per cell was established for each specimen (25 to 30 cells/specimen were scored), and it ranged from 3.0 to 9.7 in the patients and from 3.0 to 11.5 in the controls. A mean +- S.D. calculated from those means was 6.0 +-1.8 for the patients and 6.9 +-2.8 for the controls. They were not significantly different. We conclude that chemo- and radiotherapy produced no persistent DNA alterations detectable by this method. (Author abstract) (20 Refs)

19. IN VIVO SISTER CHROMATID EXCHANGE AND CELLULAR REPLICATION KINETICS OF NORMAL AND LYMPHOMA AKR BONE MARROW CELLS.

Biegel JA, Boggs SS, Conner MK
Univ. Pittsburgh Sch. Medicine, RC510 Scalfe Hall, Pittsburgh, PA, 15261
Cancer Res; 42(7):2813-2815 1982

The recent development of an AKR(Rb6.15)1Ald lymphoma model in our laboratory presents a unique means of comparing sister chromatid exchange (SCE) frequencies and cellular replication kinetics of normal and lymphoma cells in the same host environment. Lymphoma cells, distinguished from normal cells by the presence of two metacentric chromosomes, had an average cell cycle time of 8 hr compared to 11 hr for normal cells. Normal bone marrow cells from nonleukemic AKR/J, nonleukemic AKR(Rb6.15)1A1d, and tumor passage recipients had similar base-line and 1,3-bis(2-chloroethyl)-1-nitrosourea-induced SCE frequencies following exposure to 4.4 mg 1,3-bis(2-chloroethyl)-1-nitrosourea per ml and 19 hr 5-bromo-2-deoxyuridine. While base-line SCE frequencies were only slightly higher, 1,3-bis(2-chloroethyl)-1-nitrosourea-induced lymphoma cell SCE frequencies were 3x higher than normal induced SCE frequencies [34.06 +-6.6 (SE) versus 11.0 +-0.6 SCEs/cell]. (Author abstract) (11 Refs)

20. CLONAL EVOLUTION IN RELAPSE OF ACUTE LYMPHOBLASTIC LEUKEMIA.

Hayashi Y, Kaneko Y, Abe R, Sakurai M
Hematology Clinic, Saitama Cancer Center, Saitama, Japan
Rinsho Ketsueki; 22(10):1545-1551 1981

Chromosome karyotypes were determined in 22 cases of acute lymphoblastic leukemia, and sequential cytogenetic studies were performed in 5/22 (3 men, 2 women; 15-48 yr old) who had achieved remission but later had recurrence. Detailed studies were not possible in one patient who had tetraploid leukemia cells at diagnosis and after relapse. Cell samples were obtained by direct marrow aspiration or unstimulated culturing of peripheral blood. Chromosomal analysis was performed using common Giemsa staining techniques, Caspersson et al Q chromosome method, or Sanchez et al simple G-banding technique. Six clonal evolutions were observed in four patients, and death occurred soon after the discovery of the clonal evolutions. The clonal evolutions included three cases of clones derived from the original ones seen at diagnosis, a case with a clone that was completely different than the original one, a case of a clone that was a progression from diploidy to pseudodiploidy, and a case with a shift in the modal chromosome number. Modal chromosome numbers increased in one case, decreased in two, and were unchanged in two. Clonal evolution was considered to be an indicator of poor prognosis in patients with acute lymphoblastic leukemia. (27 Refs) (In JPN)

21. LEUKAEMIA OF PLATELET PRECURSORS: DIVERSE FEATURES IN FOUR CASES.

Bevan D, Rose M, Greaves M
Haematology Dept., St. George's Hosp. Medical Sch., Tooting, London, S.W. 17, England
Br J Haematol; 51(1):147-164 1982

Four patients are described with malignant cells of definite or probable megakaryocytic lineage in the bone marrow and blood. Megakaryocytic features were defined by morphological and cytochemical studies using light and electron microscopy, and in two cases by reaction with a monoclonal anti-platelet antibody, AN51. All patients had increased bone-marrow

reticulin, which developed in less than 15 mo in two cases. One of these fitted the clinical pattern of acute myelosclerosis of Lewis and Szur (now widely referred to as acute megakaryoblastic leukemia). Three cases had unique clinical features which are described in detail. There may be several variants of megakaryocytic leukemia, including chronic forms. One variant is associated with Down's syndrome (trisomy 21). (Author abstract) (50 Refs)

22. MORPHOMETRIC STUDIES OF BLOOD PLATELETS IN MYELOPROLIFERATIVE DISEASES (MEETING ABSTRACT).

Linker H, Steigleder S
Medizinische Universitatsklinik, Koln, W. Germany
Onkologie; 4(5):250 1981

Electron microscopic images of normal platelets and platelets from patients with myeloproliferative diseases were studied using a semi-automatic image analyzer (ASM, Leitz Company) with computer processing (PET 2001). The circumference and area of 1700 platelets from healthy subjects and 1600 platelets from patients with thrombocythemia, polycythemia vera, chronic myeloid leukemia, and osteomyelosclerosis were measured. As the results for healthy subjects show, section processing as well as the time of sampling and individual differences in platelet size must be taken in to account in the evaluation of any platelet section. In contrast to circumference, analysis of platelet area reveals a homogeneous distribution. In the thrombocythemic patients studied smaller platelets were usually found, in cases of polycythemia platelets were of normal size, in chronic myeloid leukemia there were various distributions and in osteomyelosclerosis platelets were usually decidedly larger especially in relation to the time of a myeloblast crisis. (no Refs) (In GER)

23. CYTOGENETIC MAPPING OF THE DUPLICATED SEGMENT OF CHROMOSOME 12 IN LYMPHOPROLIFERATIVE DISORDERS.

Gahrton G, Robert KH, Friberg K, Juliusson G, Biberfeld P, Zech L
Section Clinical Hematology and Oncology, Dept. Medicine, Huddinge Hosp., S-14186 Huddinge, Sweden
Nature; 297(5866):513-514 1982

Cytogenetic studies performed on peripheral blood lymphocytes, bone marrow cells, and spleen cells from a 56-yr-old man with lymphocytic non-Hodgkin's lymphoma indicated that the essential genes duplicated during leukemogenesis that lead to lymphoproliferative B-cell disorders characterized by trisomy of chromosome 12 are probably located on the segment q13 to q22. (10 Refs)

24. ESTABLISHMENT AND CHARACTERIZATION OF A HUMAN MYELOMA CELL LINE (KMM-1).

Togawa A, Inoue N, Shimoda M, Mannoji M, Yawata Y, Miyamoto K, Namba M
Dept. Internal Medicine, Kawasaki Medical Sch., Kawasaki, Japan
Nippon Ketsueki Gakkai Zasshi; 45(3):607-614 1982

A new cell line (KMM-1) was established from an sc plasmacytoma from a 62-yr-old man with multiple myeloma. The cells, serially cultured in suspension for 60 generations, have a doubling time of 36-40 hr. The cells have a karyotype of 47, X, -Y, 1q+,-2, +t(1:2) (cen:cen), +7, 12q+, 14q+, + mar. and have no Epstein-Barr virus determined nuclear antigen. Characteristics of other myeloma cell lines are compared with those of KMM-1. (25 Refs) (In JPN)

BIOCHEMICAL, IMMUNOLOGICAL AND OTHER CELL BIOLOGY STUDIES

25. HOMOGENEOUS POPULATIONS OF MACROPHAGES FROM HISTIOCYTIC LYMPHOMA PATIENTS AS A SOURCE OF MACROPHAGE SUBPOPULATIONS WHICH DIFFER IN IMMUNOREGULATORY PROPERTIES.

Lavie G, Shoenfeld Y, Shaklai M, Aderka D, Pick AI, Pinkhas J (c/o Shoenfeld) Dept. Internal Medicine D, Beilinson Medical Center, Petach Tigra, H 9100, Israel
Cancer; 50(1):69-77 1982

The existence of subpopulations of macrophages which express a variety of regulatory activities of other branches of the immune system is suggested in a comparative study of a human macrophage long term culture ZI and a macrophage cell line DAB-1. Both cell cultures were derived from pleural effusions of patients with diffuse histiocytic lymphoma. DAB-1 cells were found to secrete factors which strongly suppress the response of normal T and B lymphocytes to the mitogens PHA, Con-A and pokeweed mitogen (PWM) (by 96-98%) and to stimulate the cytotoxic activity of NK cells. ZI cells secrete factors which have a mild inhibitory effect on the response of lymphocytes to the T-cell mitogens PHA and Con-A and a stimulatory effect on the response to PWM, whereas very little effect could be detected on the activity of NK cells. While DAB-1 cells form large clusters during growth in culture, and are capable of inducing the formation of lymphocyte rosettes around the tumor cells, ZI cells grow as a homogeneous monolayer and could not be shown to form such rosettes. The differences in the behavior of the two cell populations suggest that the malignant transformation may have affected different subsets of macrophages in each case. Cells from histiocytic lymphoma patients may therefore be a source for homogeneous subpopulations of macrophages and their isolation and propagation in culture is one approach by which such subsets can be defined characterized and classified. The biological characterization of macrophage subsets may also be of clinical importance since a transformed subset with broad suppressor activities may lead to a violent and rapidly deteriorating course of disease, as was in the case of the patient from whom the DAB-1 cell line was derived. (Author abstract) (31 Refs)

26. THE EMERGENCE OF 6-THIOGUANINE-RESISTANT LYMPHOCYTES IN PEDIATRIC CANCER PATIENTS.

Lange BJ, Prantner JE
Div. Oncology, Children's Hosp. Philadelphia, Philadelphia, PA, 19104
Mutat Res; 94(2):487-499 1982

Emergence of 6-thioguanine (6TG)-resistant peripheral blood lymphocytes was studied in children and adolescents with Hodgkin's disease (HD) and sarcomas (SA) to investigate the role of chemotherapy, radiation therapy, and other variables inducing the 6TG-resistant phenotype. The study was conducted as a prospective study in which blood was taken from 22 patients prior to any antitumor therapy and at least 4 days after surgery and general anesthesia, and as a cross-sectional longitudinal study in which lymphocytes were first examined from 51 patients who were already receiving therapy and then at various times during or after therapy. As a group, the HD patients prior to therapy were not statistically significantly different from the controls although five patients had a variant frequency above the level of the highest control. During therapy both the median labeling index in phytohemagglutinin (PHA) was

lower than that of controls and median variant frequency was higher than control levels. However, the relative increase in 6TG-resistant variant frequency of patients on therapy was not adequately accounted for by relatively lower labeling index in PHA. SA patients did not show a significant reduction in median labeling index in PHA during therapy. Nonetheless the patients showed a significantly higher median 6TG-resistant variant frequency than controls both during and after therapy. In the prospective study, 20/22 patients showed an increase in frequency of 6TG-resistant lymphocytes during therapy; two of the samples were higher than the highest pre-therapy value for the entire group of 22 patients. Results showed that some cancer patients have abnormally high frequencies of 6TG-resistant lymphocytes, and cancer therapy either causes selection of 6TG-resistant cells or causes a phenotypic or genotypic change leading to further increases in frequencies of 6TG-resistance. (35 Refs)

27. BIOCHEMICAL CHARACTERIZATION OF SUPEROXIDE DISMUTASE ACTIVITY IN HUMAN LYMPHOCYTES AND MALIGNANT LYMPHOMAS (MEETING ABSTRACT).

Issels RD, Langfelder E, Groeneveld G, Prenninger S, Wilmanns W
Medizinische Klinik III, Klinikum Grosshadern der Universitat Munchen, Munchen, W. Germany
Onkologie; 4(5):270 1981

Dismutation of superoxide radicals, which occur as activated oxygen compounds during biochemical oxygen reduction in cells as a result of electron transfer, is catalyzed by the enzyme superoxide dismutase (SOD). This enzyme represents a defense mechanism against oxygen toxicity resulting from the formation of free oxygen radicals. Superoxide dismutase activity was measured in human T- and B-lymphocytes. Both cytoplasmic Cu/Zn-SOD and mitochondrial Mn-SOD can be detected by polyacrylamide disk gel electrophoresis and isoelectric focusing. In contrast to the lymphocytes of healthy donors, the lymphocytes of chronic lymphatic leukemia or immunocytoma patients exhibited a clearcut reduction in Mn-SOD activity. In order to characterize Cu/Zn-SOD in lymphatic tissue biochemically, the enzyme was isolated from bovine spleen and malignant lymphoma spleen by gel chromatography techniques. Mol wt, metal content and absorption spectra of the purified SOD-active protein fraction correspond to the results obtained from both known Cu/Zn-SOD's from other tissues. Pulse radiolysis measurements with purified enzymes revealed a reduced rate constant for Cu/Zn-SOD from lymphoma spleen. The biological significance of reduced superoxide dismutase activity in malignant lymphoma cells is discussed using the radiation sensitivity of these cells as an example. (no Refs) (In GER)

28. PHOSPHORYLATION OF TERMINAL DEOXYNUCLEOTIDYL TRANSFERASE IN LEUKEMIC CELLS.

Elias L, Longmire J, Wood A, Ratliff R
Dept. Medicine, Univ. New Mexico Sch. Medicine, Albuquerque, NM, 87131
Biochem Biophys Res Commun; 106(2):458-465 1982

Because of the specific involvement of protein phosphorylation in malignant transformation, the possibility that terminal deoxynucleotidyl transferase (TdT) might act as a physiological substrate for leukemic cellular protein kinase (PK) was investigated. NALM-6 (TdT-positive human lymphoblastic leukemia) cells were labeled with 32-PO4 and TdT was recovered from the lysate by phosphocellulose chromatography followed by immunoprecipitation. Electrophoresis revealed a major labeled band of mol wt 59,000 corresponding to the high mol wt form of TdT characteristic of human leukemic cells. The phosphoprotein was recovered and subjected to phosphoroaminoacid analysis, which disclosed 85% phosphoserine and 15% phosphothreonine. Purified calf thymus TdT was phosphorylated in vitro by crude and partially purified human leukemic cell PK. TdT phosphorylation by leukemic cell extracts and semi-purified PK was not stimulated by cAMP. Phosphorylation of TdT was shown to increase activity significantly, particularly in the presence of high concentrations of riboATP, as occur intracellularly. These results suggest a mechanistic link between two enzymatic systems, each of which is of largely unknown function but both of which are prominently associated with leukemia. TdT phosphorylation may be part of a coordinated general pathway pertaining to control of gene transcription and protein synthesis which is appropriately activated in proliferating normal and malignantly transformed cells. (20 Refs)

29. USE OF FLUORESCENT PROBE FOR DETECTION OF DIFFERENCES OF LEUKOCYTE MEMBRANES IN CHRONIC LEUKEMIAS.

Baglaev TN, Kalinin NN, Dobretsov GE, Kosankova ST, Vladimirov IuA
Dept. Biophysics, N. I. Pirogov Second Medical Inst., Moscow, USSR
Biull Eksp Biol Med; 93(4):35-37 1982

To evaluate the differences between the membranes of normal lymphocytes and leukemic cells, peripheral blood leukocytes from 6 patients with chronic myeloid leukemia (CML), 5 patients with chronic lymphoid leukemia (CLL), and 12 healthy controls were stained with the fluorescent probe 3-methoxybenzanthrene. The mean intensity of fluorescence in CML (71.0 units) was significantly greater than that in CLL (34.0) and in healthy controls (32.0). (9 Refs) (In RUS)

30. INTRACELLULAR GLYCOLYTIC ENZYMES IN ACUTE LEUKEMIA (MEETING ABSTRACT).

Ho AD, Flehn W, Hunstein W
Medizinische Universitats-Poliklinik, Heidelberg, W. Germany
Onkologie; 4(5):278 1981

The glycolytic enzyme phosphohexose isomerase (PHI) and lactate dehydrogenase (LDH) were analyzed in the leukemia cells and partly in the plasma as well of 13 patients with acute myeloid leukemia (AML), 7 patients with acute lymphoblastic leukemia (ALL) and 3 patients with chronic myeloid leukemia in blast transformation (BT/CML). Both intracellular and plasma LDH activity was higher in the patients than the controls (7 in number) (p less than 0.05). There were no significant differences among the 3 groups of patients (AML, ALL and BT/CML) however. Intracellular PHI activity was significantly higher in AML patients (median equals 55 mU/10(6) cells) than in patients with ALL (median equals 25 mU/10(6) cells) (p less than 0.01). The difference becomes still clearer when the LDH/PHI index is compared among the 3 groups. Patients with AML or BT/CML have a highly significantly lower value (median equals 1.25 and 0.625, respectively) than patients with ALL (median equals 2.25) (p less than 0.005). (no Refs) (In GER)

31. REDUCED AMOUNTS OF PLATELET 5-HYDROXYTRYPTAMINE IN MYELOPROLIFERATIVE DISORDERS.

Okamoto S, Nishimura J, Motomura S, Ibayashi H
Third Dept. Internal Medicine, Kyushu Univ., Fukuoka, Japan
Nippon Ketsueki Gakkai Zasshi; 45(1):142-145 1982

The amounts of 5-HT in platelets from 16 normal subjects and 16 patients with MPD including CML, polycythemia vera and essential thrombocythemia were estimated fluorometrically, after 5-HT was concentrated and purified by Amberlite resin. In patients with MPD, the amount of platelet 5-HT was significantly lower than in normal subjects (p less than 0.001). The amount of 5-HT did not correlate with platelet count in PRP, but had a good relationship to that of ADP. The reduced amount of platelet 5-HT in MPD patients was considered to be due to decreased storage pool. (Author abstract) (11 Refs)

32. ANALYSIS OF LOW NATURAL KILLER CELL ACTIVITY IN 89SR-TREATED MICE.

Mellen PF, Lust JA, Bennett M, Kumar V
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Eur J Immunol; 12(5):442-445 1982

Treatment of mice with the long-lived bone-seeking radioisotope 89Sr results in the selective irradiation and destruction of the bone marrow. This is accompanied by a marked reduction in natural killer cell activity against YAC-1 lymphoma [NK(YAC-1)]. To test for the presence of cellular suppressors of NK(YAC-1) in 89Sr- treated mice, in vitro and in vivo cell mixture protocols were used. In vitro, we did not observe any specific inhibitory effect of spleen cells from 89Sr-treated mice on NK(YAC-1) activity of normal spleen cells. The NK(YAC-1) activity of 89Sr-treated mice, measured in vivo by their ability to clear radiolabeled YAC-1 cells from the lungs, was impaired. However, spleen cells from 89Sr-treated mice, when adoptively transferred with normal spleen cells, failed to inhibit the NK(YAC-1) activity of the latter in the lung clearance assay. Further, when normal spleen cells were injected into 89Sr-treated mice, the ability of the transferred cells to mediate in vivo activity was not suppressed in the 89Sr-treated host. These experiments support the suggestion that the low NK(YAC-1) activity in 89Sr-treated mice is not mediated by suppressor cells, but may be due to the destruction of the marrow microenvironment which is essential for the generation of functional NK(YAC-1) cells. (Author abstract) (22 Refs)

EXPERIMENTAL STUDIES INVOLVING CHEMICAL AGENTS AND IRRADIATION

33. REPAIR OF DNA ALKYLATION INDUCED IN L1210 LEUKEMIA AND MURINE BONE MARROW BY THREE CHLOROETHYLNITROSOUREAS.

Ahlgren JD, Green DC, Tew KD, Schein PS
Div. Medical Oncology, Georgetown Univ. Hosp., 3800 Reservoir Road, N.W., Washington, DC, 20007
Cancer Res; 42(7):2605-2608 1982

The removal of DNA adducts is an essential step of DNA repair following exposure to chloroethylnitrosoureas. Adduct removal was evaluated in both L1210 and murine bone marrow DNA for lesions induced by three chloroethylnitrosoureas. 1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea, a marrow-toxic agent with high carbamoylating activity, was not removed in either system for at least 6 to 12 hr. These results were compared with those obtained with two glucose-linked chloroethylnitrosoureas, chlorozotocin and 1-(2-chloroethyl)-3-(beta-D-glucopyranosyl)-1 nitrosourea. Both of these agents have low marrow toxicity at therapeutic doses. Chlorozotocin, which has very low chemical carbamoylating activity, was found to permit approx 40% removal of drug-derived DNA adducts in both systems within the first 6 hr and approx 50% by 18 hr. The second glucose-linked analog, 1-(2-chloroethyl)-3-(beta-D-glucopyranosyl)-1 nitrosourea, has relatively high carbamoylating activity and was found to inhibit early removal of DNA adducts as effectively as does 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea. It would thus appear that the selective marrow-sparing property of the sugar-linked chloroethylnitrosoureas is not dependent upon carbamoylation-mediated differences in the rate and extent of DNA adduct removal. In view of the comparable therapeutic activity of the three drugs for L1210 leukemia, therapeutic efficacy does not appear to be impaired by the increased rate of adduct removal observed with chlorozotocin in this system. (Author abstract) (18 Refs)

34. EFFECT OF SERA FROM LEUKEMIC MICE ON MITOGEN INDUCED BLASTOGENESIS OF LYMPHOCYTES FROM SYNGENIC NORMAL MICE.

Bansal MP, Kalla NR, Kanwar KC
Dept. Biophysics, Panjab Univ., Chandigarh, India
Indian J Cancer; 19(2):103-106 1982

Transformation of lymphocytes by phytohemagglutinin (PHA) was evaluated in ICRC and Swiss mice. In in vitro studies, an inhibitory factor(s) for PHA-induced transformation of lymphocytes was detected in the serum of ICRC mice with leukemia induced by 3-methylcholanthrene and 7,12-dimethylbenz(a)anthracene. (21 Refs)

35. INDUCTION OF CHROMOSOME ABERRATIONS IN HUMAN LYMPHOCYTES BY RADIOMIMETIC SUBSTANCES (BLEOMYCIN AND PHLEOMYCIN) (MEETING ABSTRACT).

Scheid W, Traut H
Institut fur Strahlenbiologie, Universitat Munster, Munster, W. Germany
Molecular and Cellular Mechanisms of Irradiation, March 17-19, 1982, Neuherburg, W. Germany. Gesellschaft fur Strahlen und Umweltforschung MBH 65 pp., 1982.

The antibiotics bleomycin (BLM) and phleomycin (PLM) belong to the very small number of chemical substances which, like ionizing radiation, in addition to chromatid aberrations, induce chromosome aberrations as well. We investigated the induction of chromosome aberrations (dicentric chromosomes, ring chromosomes) in human lymphocytes by BLM and PLM. The av number of dicentric chromosomes per cell was 1.057 (BLM) and 1.273 (PLM). The concentrations (300 ug/ml) and exposure time (3 h) were the same in both series. The BLM-value obtained by Dresp et al for the same concentration is somewhat lower (0.420). In agreement with the results of the BLM studies of Dresp et al, the observed intercellular distribution of dicentric chromosomes in both the BLM and PLM series deviates from chance distribution (Poisson) ('overdispersion'). The proper chance distributions for both these distributions as well as for the distributions obtained by Dresp et al (several BLM concentrations) were calculated. In every case the same characteristic pattern was produced for the deviations

of the observed frequencies from the theoretical. This 'deviation pattern' can in principle be interpreted in 2 different ways: (1) the BLM (PLM) molecules are randomly distributed on the cells, each molecule, however, tends to induce more than 1 aberration similar to the effects of dense ionizing particles. The linear relationship between aberration frequency and BLM concentration obtained by Dresp et al are in accordance with this conception. (2) The lymphocytes treated with BLM (PLM) consist of at least 2 subpopulations with different sensitivity with respect to the induction of chromosome aberrations. Such differences in sensitivity would however exist only for chemical noxae and not for ionizing radiation, since chance intercellular distribution of x-ray induced aberrations has been reported by different authors. Our results are at variance with mutagenicity studies in Drosophila in which BLM proved quite active and PLM, on the other hand, completely inactive. This demonstrates how important it is to perform mutagenicity testing with the most varied test systems possible. (no Refs) (In GER)

EXPERIMENTAL STUDIES: DNA TUMOR VIRUSES

36. HUMAN LYMPHOMA-LYMPHOMA HYBRIDS AND LYMPHOMA-LEUKEMIA HYBRIDS. I. ISOLATION, CHARACTERIZATION, CELL SURFACE MARKERS, AND B-CELL MARKERS.

Zeuthen J, Klein G, Ber R, Masucci G, Bisballe S, Povey S, Terasaki P, Ralph P
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JNCI; 68(2):179-195 1982

Four new somatic cell hybrids were obtained by fusion of various Burkitt's lymphoma (BL)-derived cell lines that had different selective markers: Raji-P3HR-1, Daudi-Raji, and a P3HR-1-P3HR-1 'autohybrid' derived from two P3HR-1 sublines. In addition, a hybrid was was obtained between the Daudi (BL) line and the human leukemia cell line K562. The hybrids were extensively characterized by means of chromosome, isozyme, and HLA surface markers. The phenotypic differences between the parent cell lines allowed some conclusions with respect to the expression of latent Epstein-Barr virus (EBV) genomes, C3 and EBV receptors, and of immunoglobulin and beta 2-microglobulin-HLA expression as well as the influence of the leukemia cell (K562) genome on B-cell properties in the Daudi-K562 hybrid. B-cell and differentiated markers of these hybrids were characterized. High-level expression dominated for the markers C3 and EBV receptors, which showed a good correlation coefficient of 0.84, as was true for Fc receptors and surface immunoglobulin. The Daudi-K562 hybrid showed loss of all B-cell markers but retention of the leukemia cell markers (eg, hemoglobin synthesis). (Author abstract) (59 Refs)

37. HUMAN LYMPHOMA-LYMPHOMA HYBRIDS AND LYMPHOMA-LEUKEMIA HYBRIDS. II. EPSTEIN-BARR VIRUS INDUCTION PATTERNS.

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Dept. Tumor Biology, Karolinska Institutet, S-104 01 Stockholm 60, Sweden
JNCI; 68(2):197-202 1982

In addition to the spontaneous expression of markers of the early and late phases of the viral cycle [Epstein-Barr virus (EBV), early viral cycle antigens (EA), and viral capsid antigen (VCA)] by a panel of hybrid cell lines derived by fusion of human hematopoietic cell lines, the induction of these markers by three chemical inducers [5-iodo-2'-deoxyuridine, the tumor promoter 12-O-tetradecanoylphorbol 13-acetate (TPA), and sodium butyrate] were analyzed. A variant of the prototype producer of lytic EBV, P3HR-1 (PICAT) was observed to show consistent low spontaneous and induced production of EA and VCA as compared to the P3HR-1 line from which it was derived. An 'autohybrid' (PICATPO-1) between these two lines showed a low production of VCA. Hybrids between Raji and P3HR-1 sublines (RUD-PICAT-1 and RUDPUT-2) showed reduced expression of EBV antigens. Both hybrids were capable of VCA expression, in contrast to the Raji parent that expressed EA but not VCA. A new Raji-Daudi hybrid (DITRUD-1) expressed spontaneous and induced EA and VCA at levels intermediate between its two parents. A different type of hybrid was derived from a Daudi subline and the K562 leukemia cell line (DUTKO-1) and was found to be capable of spontaneous as well as induced EA and VCA expression. Both DUTKO-1 and DITRUD-1 were similar to Daudi in their induction profile in respect to a very low response to TPA. (Author abstract) (20 Refs)

38. EPSTEIN-BARR VIRUS (EBV)-LYMPHOID CELL INTERACTIONS. II. THE INFLUENCE OF THE EBV REPLICATION CYCLE ON NATURAL KILLING AND ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY AGAINST EBV-INFECTED CELLS.

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Clin Exp Immunol; 48(3):589-601 1982

We investigated the influence of the Epstein-Barr virus (EBV) replication cycle on natural killing (NK) activity and antibody-dependent cellular cytotoxicity (ADCC) against EBV-infected cells. Peripheral blood lymphocytes from healthy EBV-seropositive and -seronegative donors were separated on Ficoll-Hypaque gradients and used as effector cells in the standard 51Cr release assay to measure NK and ADCC. EBV-genome positive RAJI and DAUDI cells superinfected with either the non-transforming P3HR-1 EBV or the transforming B95-8 EBV were used as targets. The results obtained show that most normal individuals have ADCC and NK activity against P3HR-1 EBV-infected RAJI cells. Both the cytotoxic activities increased with the proportional increase in effector/target (E/T) ratios, assay incubation time, dose of the infecting virus and the time of pre-infection with EBV. Moreover, the data obtained indicate that different immune mechanisms are effective at different stages of the virus replication cycle. During the early stages of virus replication, EBV-superinfected cells are more susceptible to ADCC than to NK, whereas in later stages the susceptibility to NK is increased significantly and appears to play a more dominant role. The nature of the target cells or the strain of EBV used to superinfect these targets did not influence their susceptibility to ADCC and NK activity; however some quantitative differences were found. Using metabolic inhibitors such as cytosine arabinoside, phosphonoacetic acid, actinomycin D, cycloheximide and puromycin, it was found that new DNA synthesis is not essential but some RNA and protein synthesis is necessary, late in the viral cycle, for the superinfected cells to become susceptible to NK and ADCC. (Author abstract) (34 Refs)

39. CHARACTERIZATION OF PERIPHERAL LYMPHOID CELLS (DOWNEY CELLS) DURING INFECTIOUS MONONUCLEOSIS (IM), USING MONOCLONAL ANTIBODIES (MEETING ABSTRACT).

Fjelde A, Ozer H, Kellam J, Bennett P
Roswell Park Memorial Institute, Buffalo, NY, 14263
In Vitro; 18(3,part2):309 1982

The present study is part of a project concerning the relationship of IM and human lymphoma-leukemia, in which we have reported the presence of Paul-Bunnell (PB) antigen, the antibody which is present in high titer and diagnostic for IM. The present study is an investigation of the nature of the peripheral blood cell population in terms of surface antigens, using monoclonal antibodies and the cell sorter. A preliminary study using other methods showed an absolute increase in T lymphocytes. During early (1st week) IM, we found that a high percentage of responders to monoclonal antibodies represented T cells, suppressor-cytotoxic (SC) cells and E rosette responding cells. At 1 month peripheral T cells (OKT-3) remained high, but all other values returned to normal or below. Response to OKT-4 antibodies representing helper-inducer T cells (H), was low at both periods. Values for OKT-6, 8, 11a OKIa and OKM1 were above normal at 1 week, but returned to normal at 1 month. The H/SC ratio was less than 1 at both periods, demonstrating an inversion of the normal values. Induction of IM by EM virus infection of B lymphocytes causes T cell reactive Downey cell proliferation, apparently representing a control system. (no Refs)

EXPERIMENTAL STUDIES: RNA TUMOR VIRUSES

40. INTERNAL ORGANIZATION OF ENDOGENOUS PROVIRAL DNAS OF XENOTROPIC MURINE LEUKEMIA VIRUSES.

Hoggan MD, Buckler CE, Sears JF, Chan HW, Rowe WP, Martin MA
Lab. Viral Diseases, Natl. Inst. Allergy and Infectious Diseases, Bethesda, MD, 20205
J Virol; 43(1):8-17 1982

The internal organization of endogenous xenotropic murine leukemia virus proviruses was determined in a series of blot hybridization experiments in which DNA from several different inbred mouse strains, digested with restriction enzymes known to cleave xenotropic proviral DNAs at least twice, was annealed to generalized murine leukemia virus or xenotropic env-specific DNA probes. Comigrating bands of variable intensity which hybridized to the xenotropic env probe were identified in all inbed mouse DNA preparations. At least seven classes of endogenous xenotropic proviral DNA with respect to SacI cleavage maps were detected in mouse DNA. Two of the seven classes were indistinguishable from proviruses associated with known infectious xenotropic murine leukemia viruses. These results are consistent with the existence of related but organizationally distinct families of endogenous xenotropic proviral DNA that are present in different relative abundances in mouse genomic DNA. (Author abstract) (20 Refs)

41. ORGANIZATION, DISTRIBUTION, AND STABILITY OF ENDOGENOUS ECOTROPIC MURINE LEUKEMIA VIRUS DNA SEQUENCES IN CHROMOSOMES OF MUS MUSCULUS.

Jenkins NA, Copeland NG, Taylor BA, Lee BK
Jackson Lab., Bar Harbor, ME, 04609
J Virol; 43(1):26-36 1982

The endogenous ecotropic murine leukemia virus DNA content and integration sites were characterized for 54 inbred strains and substrains of mice by restriction enzyme digestion, Southern blotting, and hybridization with an ecotropic murine leukemia virus DNA-specific probe. More than 75% of these strains carried endogenous ecotropic proviruses which were located in at least 29 distinct integration sites in chromosomes of Mus musculus. Fourteen of these proviruses have been assigned specific locus designations. Most, but not all, of the endogenous ecotropic proviruses were structurally indistinguishable by this analysis from the prototype AKR ecotropic virus, and the distribution of these proviruses followed known relationships among the inbred strains and substrains of mice. These results suggest that, in general, viral DNA integration preceded the establishment of inbred mouse strains and that these integrations are relatively stable. (Author abstract) (42 Refs)

42. LOSS OF VIRAL GENE EXPRESSION AND RETENTION OF TUMORIGENICITY BY ABELSON LYMPHOMA CELLS.

Grunwald DJ, Dale B, Dudley J, Lamph W, Sugden B, Ozanne B, Risser R
McArdle Lab. Cancer Res., Univ. Wisconsin, Madison, WI, 53706
J Virol; 43(1):92-103 1982

Lymphomas induced by the Abelson murine leukemia virus (A-MuLV) were examined for the expression of biochemical and biological markers associated with A-MuLV transformation before and after in vivo growth in genetically distinguishable host mice. Although all tumors and clonal lines derived from them initially expressed the A-MuLV-encoded gag fusion protein p160, they ceased synthesis of this molecule after several weeks of growth in vivo as ascites tumors. Transplanted clonal lines continued to express the alloantigenic marker H-2b and the isoenzyme marker Gpi-1b of the donor tumor cells, indicating that the cells were of donor and not host origin. Examination of cellular DNA obtained from p160-positive and derivative p160-negative lines indicated that p160-negative clones had lost A-MuLV-specific proviral sequences as detected by hybridization with several probes. Although the clonal lines no longer expressed p160, they retained their malignant phenotype and continued to express the Abelson antigen, a cell surface marker associated with A-MuLV lymphomagenesis. Continued expression of the A-MuLV genome was not required for maintenance of oncogenic potential under these conditions of in vivo tumor growth. (Author abstract) (38 Refs)

43. SHUT-DOWN OF VIRUS SYNTHESIS DURING PROGRESSION OF ERYTHROLEUKEMIA INDUCED BY FRIEND VIRUS IN MICE.

Yoosook C
Dept. Microbiology, Faculty Science, Mahidol Univ., Rama 6 Road, Bangkok 4, Thailand
Int J Cancer; 29(6):659-665 1982

Infection of (C57BL/6 x DBA/2)F1 (BDF1) mice with 2,500 FFU of Friend virus complex (FV) resulted in erythro-

leukemia followed by recovery, at which time virus could not be detected in the spleens of mice, and with splenomegaly (progressor mice) or without splenomegaly (regressor mice). Progressor and regressor mice developed equally high amounts of FV-neutralizing activity in their sera. Progressor mice contained cells capable of producing virus, despite the lack of viral envelope antigen(s) in their spleens. The tropism of FV recoverable from the spleens of secondary recipients, injected with spleen cells from progressor mice, did not show any change, although the viral genome was present in Fv-1-restrictive host for at least 7 wk. When the number of spleen colony-generating cells was enumerated, by the spleen colony assay, the frequency in normal syngeneic and in allogeneic hosts was approx the same at the early stage of erythroleukemia but was about 1,000 times higher in the syngeneic recipients during leukemia progression. These spleen colony-generating cells were considered to be FV-transformed cells capable of self-renewal and capable of generating infectious centers (IC), respectively. Most of these transformed cells might be non-producer leukemia cells. (Author abstract) (28 Refs)

44. NUCLEOTIDE SEQUENCE OF THE TRANSFORMING GENE OF AVIAN MYELOBLASTOSIS VIRUS.

Rushlow KE, Lautenberger JA, Papas TS, Baluda MA, Perbal B, Chirikjian JG, Reddy EP
(c/o Papas) Lab. Molecular Oncology, NCI, Bethesda, MD, 20205
Science; 216(4553):1421-1423 1982

Avian myeloblastosis virus is defective in reproductive capacity, requiring a helper virus to provide the viral proteins essential for synthesis of new infectious virus. This virus arose by recombination of the nondefective helper virus and host cellular sequences present within the normal avian genome. These latter sequences are essential for leukemogenic activity. The complete nucleotide sequence of this region is reported. Within the acquired cellular sequences there is an open reading frame of 795 nucleotides starting with the initiation codon ATG (adenine, thymine, guanine) and terminating with the triplet TAG. This open reading frame could code for the putative transforming protein of 265 amino acids with a mol wt of approx 30,000. (Author abstract) (17 Refs)

45. MORPHOLOGICAL, IMMUNOLOGICAL, AND BIOCHEMICAL ANALYSES OF CHICKEN SPLEEN CELLS TRANSFORMED IN VITRO BY RETICULOENDOTHELIOSIS VIRUS STRAIN.

Shibuya T, Chen I, Howatson A, Mak TW
Dept. Medical Biophysics, Ontario Cancer Inst., Univ. Toronto, Toronto, M4X 1K9, Canada
Cancer Res; 42(7):2722-2728 1982

Reticuloendotheliosis virus strain T (REV-T) is a highly oncogenic avian retrovirus which causes a rapid neoplastic disease of the lymphoreticular system. We derived six cell lines from chicken spleen cells infected with REV-T. These cells can produce both the REV-T and its associated reticuloendotheliosis helper virus, REV-A. Histochemical analyses of these cells indicate that, while they are not stained by benzidine, peroxidase, beta-glucuronidase or acid alpha-naphthyl acetate esterase, they contain a high proportion (95%) of cells positive for acid phosphatase. Light and electron microscopic studies of these cells also revealed morphologies of lymphoblasts or activated lymphocytes with irregular nuclei and dispersed chromatin. Immunochemical analyses indicate that essentially all (90 to 100%) of the cells contain the surface marker Ia, but no cytoplasmic immunoglobulin M and immunoglobulin G could be detected by immunofluorescence staining. Results also show that some of these cell lines contain a low level of terminal transferase, and a proportion of these cells can be stained by an antiserum directed against chicken bursa cells. These results are consistent with the conclusion that the cells transformed by the highly oncogenic REV-T are lymphoid in nature. In addition, at least some of these cell clones may contain features characteristic of activated B-lymphocytes. Analysis of these cell clones indicates that some cell lines contain an adherent and nonadherent population with some differences in morphologies. In addition, electron microscopic examination revealed that, while the nonadherent cells are actively producing Type C viruses, Type C viruses are either absent or very rare in the adherent cell populations. These results support the conclusion that some of these cell lines are heterogeneous and contain subpopulations of cells with differences in their ability to produce viruses. (38 Refs)

46. TRANSCRIPTS FROM THE CELLULAR HOMOLOGS OF RETROVIRAL ONCOGENES: DISTRIBUTION AMONG CHICKEN TISSUES.

Gonda TJ, Sheiness DK, Bishop JM
Dept. Microbiology and Immunology, Univ. California, San Francisco, CA, 94143
Mol Cell Biol; 2(6):617-624 1982

RNA transcribed from each of the four c-onc genes c-myb, c-myc, c-erb, and c-src was quantified in a variety of tissues and cells by dot-blot assay with standardized avian myeloblastosis virus (AMV) 70S virion RNA. Cells examined for levels of c-onc RNAs included fibroblasts, whole embryo, yolk sac, Marek's disease-transformed cells (MSB-1), avian erythroblastosis virus (AEV) erythroblasts and fibroblasts and AMV myeloblasts. Transcription from each c-onc gene was detected (as c-myc, c-erb, and c-src RNA) in nearly all cells and tissues examined, but significant c-myb transcription was detected only in hemopoietic cells. The amount of c-onc RNAs varied, relatively little variation was observed in c-erb levels, a greater range in c-myc and c-src RNA levels was noted, and the greatest variations were exhibited by c-myb levels. Organs expressing the highest levels of c-myb (bone marrow, yolk sac, thymus) are major hemopoietic organs of the chicken, suggesting that c-myb may be expressed in immature hemopoietic cells. The high level of c-myb expression found in AEV-transformed erythroblasts suggests that c-myb function is not restricted to myelomonocytic cells. No obvious correlation existed between susceptibility to transformation and c-onc expression. (40 Refs)

47. IMMUNOPATHOLOGY OF B-CELL LYMPHOMAS INDUCED IN C57BL/6 MICE BY DUALTROPIC MURINE LEUKEMIA VIRUS (MULV).

Pattengale PK, Taylor CR, Twomey P, Hill S, Jonasson J, Beardsley T, Haas M
Dept. Pathology, Univ. Southern California Sch. Medicine, 2025 Zonal Ave., Los Angeles, CA, 90033
Am J Pathol; 107(3):362-377 1982

Combined clinicopathologic and immunomorphologic evidence is presented that would indicate that a murine leukemia virus (MuLV) with the dualtropic host range is capable of producing a clinically malignant lesion composed of immunoblasts and associated plasma cells in C57BL/6 mice. This process, morphologically diagnosed as an immunoblastic lymphoma of B cells using standard histopathologic criteria, was found to be distinctly polyclonal with regard to immunoglobulin (Ig) isotype when analyzed for both surface and cytoplasmic Ig. Fur-

ther studies demonstrated that this clinicopathologically malignant, dualtropic MuLV-induced, polyclonal immunoblastic lymphoma of B cells in C57BL/6 mice was normal diploid and unable to be successfully transplanted to nonimmunosuppressed syngeneic recipients. Although all serum heavy and light chain components were found to be progressively elevated as the tumor load increased, the polyclonal increase in serum immunoglobulins was most pronounced for mu heavy and kappa light chains (ie, mu greater than gamma2A greater than alpha greater than gamma 2B greater than gamma1; kappa greater than lambda). The dissociation of clinicopathologic and biologic criteria for malignancy in the presently described dualtropic (RadLV) MuLV-induced B-cell lesion is sharply contrasted with the thymotropic (RadLV) MuLV-induced T-cell lymphoblastic lymphoma in C57BL/6 mice. This process is also a clinicopathologically malignant lesion but, when one uses biologic criteria, is found to be distinctly monoclonal, aneuploid, and easily transplanted to nonimmunosuppressed syngeneic recipients. The close clinicopathologic and biologic similarities of the dualtropic MuLV-induced animal model to corresponding human B-cell lymphoproliferative diseases are stressed. (Author abstract) (46 Refs)

48. DETECTION OF A COMMON ANTIGEN ON MURINE B CELLS AND LYT-2+ T CELLS BY A RAT MONOCLONAL ANTIBODY, 14D10.

Kung JT, Sharrow SO, Mage MG, Paul WE
Lab. Immunology, NIH, Natl. Inst. Allergy and Infectious Diseases, Building 10, Room 11N311, Bethesda, MD, 20205
J Immunol; 129(1):81-86 1982

This paper reports the production of a rat monoclonal antibody, 14D10, which recognizes a determinant shared between B cells and Lyt-2+ T cells. Three subpopulations of spleen cells were defined based on the density of bound 14D10. They have been designated 14D10-SP (strongly positive), 14D10-WP (weakly positive), and 14D10-N (negative). Dual parameter immunofluorescence studies showed that 90% of 14D10-SP cells are IgM+ cells and more than 92% IgM+ cells are 14D10-SP. Of 14D10-WP cells, approx 60% are Lyt-1+2+ T cells and less than 10% are Igm+ cells. However, most (greater than 90%) of Lyt-2+ T cells are reactive with 14D10. Staining of purified populations of Lyt-2+ and Lyt-2(-) T cells with fluoresceinated 14D10 also showed greater than 90% of Lyt2+ T cells to be 14D10+, and fewer than 10% of Lyt-2(-) T cells are 14D10+. Mouse thymus contained very few (approx = 5%) 14D10+ cells. Analysis of bone marrow cells shows almost all small cells to be 14D10+. Six Abelson virus-transformed cell lines all express the antigen recognized by 14D10. (Author abstract) (19 Refs)

REVIEWS AND OTHER RELATED STUDIES

49. PROPOSALS FOR THE CLASSIFICATION OF THE MYELODYSPLASTIC SYNDROMES.

Bennett JM, Catovsky D, Daniel MT, Flandrin G, Galton DA, Gralnick HR, Sultan C, French-American-British Co-Operative Group (c/o Catovsky) MRC Leukaemia Unit, Royal Postgraduate Medical Sch., Ducane Road, London W12 0HS, England
Br J Haematol; 51(2):189-199 1982

New diagnostic criteria for the diagnosis of the various myelodysplastic syndromes (MDS) are proposed, and a detailed description is given of the features that may help define MDS. Five MDS are described: (1) refractory anemia (RA), (2) RA with ring sideroblasts, (3) RA with excess of blasts (RAEB), (4) chronic myelomonocytic leukemia (CMML), and (5) RAEB 'in transformation'. One of the main distinguishing features of these conditions is the proportion of blast cells in the peripheral blood (PB) and/or bone marrow (BM). The morphological features of the blast cells that are of diagnostic importance have been redefined. In RA, with or without ringed sideroblasts, there are fewer than 1% of blasts in the PB and fewer than 5% in the BM; RAEB is defined as having between 5% and 20% of blasts in the BM and fewer than 5% in the PB; RAEB in transformation (a newly defined category) will be considered when any one of the following features is present: (i) more than 5% of blasts in the PB, (ii) 20-30% in the BM, and (iii) the presence of Auer rods in granulocyte precursors in BM or PB. In accordance with these newly defined criteria, it is now proposed that over 30% of bone marrow blasts will suffice for the diagnosis of acute myeloid leukemia (AML) in any of its forms (M1-M6). The proposed descriptions of the MDS should facilitate the interpretation of data emerging from cytogenetic and bone marrow culture studies and the search for features of possible prognostic significance. Recognition of the new category, RAEB in transformation, may throw light on the pathogenesis of AML. (Author abstract) (7 Refs)

50. LEUKAEMIA: A SERIES OF WORKSHOPS ON THE BIOLOGY OF HUMAN CANCER. REPORT NO. 14.

Warner NL, Metcalf D
No affiliation given
UICC Tech Rep Ser 61: 232 pp., 1981.

The biological basis of leukemia is discussed under the following headings: hemopoietic cell proliferation and differentiation (multipotential hemopoietic stem cells, progenitor cells, morphologically recognizable cells, control of differentiation and proliferation, and analysis of normal and malignant hemopoietic cell differentiation), clinical nature and classification of human leukemia (surface marker characterization, acute leukemia, chronic leukemia, and abnormal physiology), chromosomal and clonal analysis of leukemia (chromosome changes in leukemia and clonal nature of leukemia), etiology of leukemia (radiation and leukemia, induction of leukemia by chemical carcinogens, retroviruses and leukemogenesis, other etiological factors in leukemogenesis, and epidemiological patterns of leukemia), and regulation of leukemic cell growth (leukemic cell growth in vitro, regulatory control of myeloid leukemic cells, and marrow transplantation). (581 Refs)

51. HEMATOLOGIC MALIGNANCIES IN THE ADULT.

Newcom SR, Kadin ME
Section Medical Oncology, Univ. Oregon Health Sciences Center, Portland, OR
Hematologic Malignancies in the Adult. Menlo Park, CA, Addison-Wesley Publishing Company Medical/Nursing Division, 230 pp., 1982.

Hematologic malignancies in the adult are reviewed. Topics include the pre-leukemic syndrome (hemopoietic dysplasia), acute leukemia in the adult, chronic myelogenous leukemia, myeloproliferative disorders, plasma cell disorders, Hodgkin's disease, non-Hodgkin's lymphomas, chronic lymphocytic leukemias, and uncommon lymphoproliferative disorders. Details of patient evaluation are provided, including clinical characteristics of each disorder. Current terminology or pathologic classification is included for each disease when appropriate. Knowledge regarding etiology, including known congenital and environmental causes of acute leukemia is summarized. Recent therapeutic results are tabulated. An analysis of the

value of such aspects of treatment as CNS prophylaxis, maintenance therapy, late intensification, and bone marrow transplantation is provided. The criteria for diagnosis of chronic myelogenous leukemia are presented, with attention to leukocyte alkaline phosphatase stain and the Philadelphia chromosome. Polycythemia rubra vera, myelofibrosis with agnogenic myeloid metaplasia, and primary thrombocytopenia are considered. The prognosis and results of therapy for both osseous and extramedullary plasmacytomas are presented. The potential for curability of advanced histiocytic lymphoma is analyzed, and staging and treatment recommendations are made. Unique but predictable clinical behavior of benign and malignant histiocytoses, lymphoblastic lymphoma, hairy cell leukemia, angioimmunoblastic lymphadenopathy, Lennert's lymphoma, the T-cell skin lymphomas, and Burkitt's lymphoma is discussed; the pathologic features are defined and differential diagnosis is outlined. (461 Refs)

52. CHROMOSOME ABNORMALITIES IN MALIGNANT HEMATOLOGIC DISEASES.

Rowley JD, Testa JR
Franklin McLean Memorial Res. Inst., Univ. Chicago, Chicago, IL, 60637
Adv Cancer Res; 36:103-148 1982

Recent results in the study of the role of chromosome abnormalities in malignant hematologic diseases are reviewed. Chromosome abnormalities associated with chronic myelogenous leukemia, acute nonlymphocytic leukemia (ANLL), acute lymphocytic leukemia, and polycythemia vera are described, and the implications of nonrandom changes for malignant transformation are discussed. The relatively consistent chromosome changes, especially specific translocations, that are closely associated with particular neoplasms provide convincing evidence for the fundamental role of these changes in the transformation of a normal cell to a malignant one. The number of nonrandom changes that are seen in a cancer such as ANLL suggests that a class of genes is involved. Human gene mapping makes it possible to relate the chromosomes affected by chromosome changes associated with neoplasia to specific genes they carry. Preliminary results showed that chromosomes with genes associated with nucleic acid biosynthesis, and specific regions of the chromosomes bearing these genes, were frequently involved in rearrangements associated with hematologic cancers. The goal of future studies must be to show how chromosome changes provide selected cells in certain persons with a growth advantage resulting in malignancy. (175 Refs)

53. CHROMOSOMAL ABERRATIONS IN CHRONIC B-CELL LYMPHOCYTIC LEUKEMIA.

Gahrton G, Robert KH
Dept. Medicine, Karolinska Inst., Huddinge Univ. Hosp., S-141 86 Huddinge, Sweden
Cancer Genet Cytogenet; 6(2):171-181 1982

Production, incidence, and types of chromosome aberrations in chronic B-cell lymphocytic leukemia (B-CLL) are reviewed. Of polyclonal B-cell mitogens, Epstein-Barr virus and lipopolysaccharide from E coli have been the most successful for cytogenetic analysis of B-CLL. The mitogenic responses measured by 3H-labeled thymidine incorporation into leukemic cells and the mitotic index are variable. Difficulties associated with calculating reliable incidence figures for chromosomal aberrations in B-CLL are considered. In B-CLL, both numerical and structural aberrations are found. The most common numerical aberration is an extra chromosome 12. Other aberrations include deletion of chromosome 14, translocations, deletions, and other extra chromosomes. Many of the chromosomal abnormalities seen in B-CLL have also been found in other malignant hematopoietic disorders, particularly lymphoproliferative disorders. However, the most common abnormality, the extra chromosome 12, is rare in other disorders. The biological significance and prognostic importance of chromosomal aberrations in B-CLL are discussed. (72 Refs)

54. BIOLOGY OF ESTABLISHED HUMAN LYMPHOMA CELL LINES (MEETING ABSTRACT).

Kaplan HS
Department of Radiology, Stanford University School of Medicine, Stanford, CA, 94305
In Vitro; 18(3,part2):319 1982

Beginning with the African Burkitt lymphomas, several types of diffuse lymphomas have now been established as permanent cell lines, whereas the nodular (follicular) lymphomas have proven refractory to in vitro cultivation. Limited success has been reported with the giant cells from patients with Hodgkin's disease. Clonal growth in semisolid media has also been observed, but may require special conditions. The cutaneous T cell lymphomas require supplementation with human T cell growth factor (TCGF), except for rare lymphomas which are constitutive TCGF producers. The established cell lines have been extensively characterized with respect to cell surface markers and functional attributes. In contrast to banal EBV-transformed B-lymphoblastoid lines, they are all monoclonal, remarkably stable in phenotype, and most lack EBV genomes. The criteria of neoplasia in lymphoma cell lines differ in several important respects from those of neoplasms derived from anchorage-dependent cells. (no Refs)

55. HUMAN B-CELL NEOPLASMS IN RELATION TO NORMAL B-CELL DIFFERENTIATION AND MATURATION PROCESSES.

Godal T, Funderud S
Lab. Immunology, Dept. Pathology, Norwegian Radium Hosp., Oslo, Norway
Adv Cancer Res; 36:211-255 1982

Functional studies related to human B-cell neoplasias are reviewed. The B-cell system is described, including its immunoglobulin (Ig) gene organization and expression, repertoire expression, surface markers related to B-cell development, and regulation of B-cell function. General features of B-cell neoplasms, the relationships of the neoplasms to B-cell development, clinical prognosis determinants, and subsets and neoplasms in the B-cell compartment are discussed. Topics discussed include simultaneous expression of IgM and IgD; expression of surface and other Ig classes and the functions of surface Ig; complement receptors and B-cell differentiation; B-cell proliferation and antibody production; and maturation of B-cell neoplasms. Chronic lymphocytic leukemia (CLL), acute lymphoblastic leukemia (ALL), and non-Hodgkins lymphomas (NHL) are discussed. Both in mouse and man there is considerable evidence for the existence of distinct functional subsets of cells in the B-cell compartment. B-cells are assumed to come from a single lineage, and during most stages of development they have multiple choices for further development, ie, they retain differentiation potential. On this basis a model of neoplastic transformation is proposed to account for the existence of multiple myelomas, NHL, CLL, and ALL. (285 Refs)

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1. TOXICITY OF POLYBROMINATED BIPHENYLS (PBBS) IN DOMESTIC AND LABORATORY ANIMALS.
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Natl. Inst. Environmental Health Sciences, Post Office Box 12233, Research Triangle Park, NC, 22709
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2. CHLOROFORM: A REVIEW OF ITS METABOLISM, TERATOGENIC, MUTAGENIC, AND CARCINOGENIC POTENTIAL.
Davidson IW, Sumner DD, Parker JC
(c/o Parker) ECAO, Environmental Protection Agency, MD-52, Research Triangle Park, MD, 27711
Drug Chem Toxicol; 5(1):1-87 1982

3. FORMALDEHYDE IN PRESENT-DAY ENVIRONMENTAL TOXICOLOGY.
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IN: 148th National Meeting of the American Association for the Advancement of Science, January 3-8, 1982, Washington, D.C American Association for the Advancement of Science 182 pp., 1982.

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22. METABOLIC EPIDEMIOLOGY OF LARGE BOWEL CANCER.
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24. TRENDS IN THE INCIDENCE OF GASTRIC CARCINOMA (MEETING ABSTRACT)
Nobrega FT
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Eleventh Annual William Beaumont Gastrointestinal Symposium, March 24-26, 1982, El Paso, Texas. William Beaumont Army Medical Center 56 pp., 1982.

25. CANCER IN INFLAMMATORY BOWEL DISEASE.
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EPIDEMIOLOGY AND ETIOLOGY OF HUMAN LYMPHORETICULAR MALIGNANCIES: VIRAL STUDIES

1. EPSTEIN-BARR VIRUS-INDUCED DISEASES IN BOYS WITH THE X-LINKED LYMPHOPROLIFERATIVE SYNDROME (XLP). UPDATE ON STUDIES OF THE REGISTRY.

Purtilo DT, Sakamoto K, Barnabei V, Seeley J, Bechtold T, Rogers G, Yetz J, Harada S, XLP Collaborators
Dept. Pathology and Lab. Medicine, Univ. Nebraska Medical Center, 42nd and Dewey Ave., Omaha, NE, 68105
Am J Med; 73(1):49-56 1982

Analyses of 100 subjects with the X-lined lymphoproliferative syndrome (XLP) in 25 kindreds revealed four major interrelated phenotypes: infectious mononucleosis, malignant B-cell lymphoma, aplastic anemia, and hypogammaglobulinemia. Eighty-one of the patients died. Two male subjects were asymptomatic but showed immunodeficiency to Epstein-Barr virus (EBV). Seventy-five subjects had the infectious mononucleosis phenotype and concurrently, 17 subjects of this group had aplastic anemia. All subjects with aplastic anemia died

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within a wk. Aplastic anemia did not accompany hypogammaglobulinemia or malignant lymphoma phenotypes. Hypogammaglobulinemia had been detected before infectious mononucleosis in three subjects, after infectious mononucleosis in five subjects, and was not associated with infectious mononucleosis in 11 boys with hypogammaglobulinemia. In nine subjects infectious mononucleosis appeared to have evolved into malignant lymphoma; however, the majority of patients with malignant lymphoma showed no obvious antecedent infectious mononucleosis. One subject had infectious mononucleosis following recurrent malignant lymphoma. Twenty-six of 35 lymphomas were in the terminal ileum. Results of immunologic and virologic studies of 15 survivors revealed combined variable immunodeficiency and deficient antibody responses to EBV-specific antigens. Mothers of boys with XLP exhibited abnormally elevated titers of antibodies to EBV. Subjects of both sexes with phenotypes of XLP should be investigated for immunodeficiency to EBV. Persons with inherited or acquired immunodeficiency may be vulnerable to life-threatening EBV-induced diseases. (Author abstract) (26 Refs)

2. MALIGNANT LYMPHOPROLIFERATIVE DISEASES INDUCED BY EPSTEIN-BARR VIRUS IN IMMUNODEFICIENT PATIENTS, INCLUDING X-LINKED, CYTOGENETIC, AND FAMILIAL SYNDROMES.

Purtilo DT
Dept. Pathology, Univ. Nebraska Medical Center, 42nd and Dewey Ave., Omaha, NE, 68105
Cancer Genet Cytogenet; 4(3):251-268 1981

An attempt is made to develop an etiologic basis for malignant lymphoproliferative disorders (LPD). Topics reviewed include infectious mononucleosis and normal immune responses; immune deficiency predisposing to fatal lymphoproliferation; X-linked LPD predisposing to fatal infectious mononucleosis and malignant lymphomas; Epstein-Barr virus-induced LPD in renal transplant recipients; ataxia telangiectasia and its relationship to immune deficiency, increased chromosomal breakage, and lymphoproliferative malignancies; familial lymphoproliferative malignancies; male predominance of lymphoproliferative malignancies; cytogenetic errors and determination of phenotypes of lymphoproliferative malignancies; masquerading malignant histiocytosis syndrome; Epstein-Barr virus and familial immunodeficiency in Hodgkin's disease; epidemiology of Hodgkin's disease; Hodgkin's disease following infectious mononucleosis; the ability of immune deficiency to virus to induce Hodgkin's disease; the relationship of immunoregulatory defects to the production of immune deficiency, autoimmunity, or malignant lymphoma; and prelymphoma syndrome. (55 Refs)

3. PERSISTENT ACTIVE INFECTION OF EPSTEIN-BARR VIRUS (EBV) IN CARRIER FEMALES OF THE X-LINKED LYMPHOPROLIFERATIVE SYNDROME (XLP).

Sakamoto K, Seeley JK, Purtilo DT
Second Dept. Surgery, Kumamoto Univ. Medical Sch., Kumamoto 860, Japan
Excerpta Med Int Congr Ser; 571:375-379 1982

Among conditions that may follow infection with Epstein-Barr virus (EBV), is malignant lymphoma in males affected by the X-linked lymphoproliferative syndrome (XLP). To test the hypothesis that the variable expression of XLP is manifested in obligate carrier females, blood from 12 obligate carrier females was studied for anti-viral capsid antigen (VCA), anti-early antigen (anti-EA) and anti-Epstein-Barr nuclear-associated antigen (EBNA). All carriers were seropositive to EBV. The reciprocal geometric mean titer for IgG anti-VCA was elevated to 570 in the carrier females compared to 100 in 24 controls. The range of anti-VCA was from 80 to 5,120. IgA class anti-VCA was found in 2/3 of the carriers. All but one of those with anti-VCA of IgA class showed anti-EA, indicative of active infection and immunodeficiency. About one-half of the carriers had persistent anti-EA antibodies. However, the anti-EBNA levels of carrier females were similar to those of the healthy controls. There was no apparent relationship between IgM level and EBV-specific antibody titers. The paradoxically elevated EBV-specific antibodies which tend to persist in obligate carriers of XLP provides an opportunity to define the immunopathology of XLP and to detect carrier females. (17 Refs)

4. EPSTEIN-BARR VIRUS ACTIVATION WITH EUPHORBIACEAE PLANT EXTRACTS: A POSSIBLE CAUSE FOR BURKITT'S LYMPHOMA AND NASOPHARYNGEAL CARCINOMA.

Ito Y, Yanase S, Morigaki T, Kishishita M
Dept. Microbiology, Faculty Medicine, Kyoto Univ., Kyoto 606, Japan
Excerpta Med Int Congr Ser; 571:423-427 1982

Speculation is raised as to whether Epstein-Barr virus-activating substances generated by Fusobacterium and other anaerobes in the mouth, and diterpene esters in Euphorbiaceae extracts with similar activity, might interact in the mouth to initiate the first step of carcinogenesis, which eventually may lead to Burkitt's lymphoma. Similar chronic inflammation in the nasal cavity and nasopharynx could serve to cause nasopharyngeal carcinoma. (2 Refs)

5. INTERACTION OF EPSTEIN-BARR VIRUS WITH LEUKAEMIC B CELLS IN VITRO. II. CELL LINE ESTABLISHMENT FROM PROLYMPHOCYTIC LEUKAEMIA AND FROM WALDENSTROM'S MACROGLOBULINAEMIA.

Finerty S, Rickinson AB, Epstein MA, Platts-Mills TA
Dept. Pathology, Medical Sch., Univ. Bristol, Bristol, England
Int J Cancer; 30(1):1-7 1982

Leukemic B-cell populations were prepared from six patients with high-count prolymphocytic leukemia (PLL) as well as from one patient with Waldenstrom's macroglobulinemia (WM) in frankly leukemic phase, and their response to in vitro Epstein-Barr (EB) virus infection was monitored in terms of expression of the virus-associated nuclear antigen EBNA and of virus-induced transformation to continuous cell lines. The individual leukemic populations, tested on several occasions, gave reproducibly different responses one from another which were not obviously related to differences either of surface immunoglobulin phenotype or of immunoglobulin secretor status in vivo. After infection, four out of six PLL populations showed either transient or a more persistent expression of EBNA, always involving a minority of the cells, with no evidence of any virus-induced transformation up to 6 wk. In contrast, two out of six PLL samples as well as the WM sample rapidly gave rise to EBNA-positive cell lines which, on the evidence both of restricted immunoglobulin class expression and of abnormal marker chromosomes, were clearly derived from the leukemic cells. Further comparative studies of such leukemic B-cell populations may help to define host cell components necessary for the triggering of EB-virus-induced cellular transformation. (Author abstract) (32 Refs)

EPIDEMIOLOGY AND ETIOLOGY OF HUMAN LYMPHORETICULAR MALIGNANCIES: OTHER STUDIES

6. DEVELOPMENT OF NON-HODGKIN'S LYMPHOMA SUBSEQUENT TO MARROW TRANSPLANTATION (MEETING ABSTRACT).

Hackman RC, Schubach WH, Neiman PE, Miller G, Thomas ED
Division of Oncology, Fred Hutchinson Cancer Research Center, Seattle, WA
71st Annual Meeting of the International Academy of Pathology (United States-Canadian Division), March 1-5, 1982, Boston, Massachusetts. International Academy of Pathology 95 pp., 1982.

We have noted the development of a malignant solid tumor in two of approximately 850 marrow allograft recipients. Both have been non-Hodgkin's lymphomas of B lymphocytes. One was an immunoblastic sarcoma identified at autopsy in a 5-year-old male 56 days after marrow grafting for acute lymphoblastic leukemia. The donor was his sister who was HLA-mismatched at one A locus. Moderate acute graft versus host disease (GVHD) had been documented by skin biopsy. Immunoperoxidase staining of the tumor demonstrated only intracytoplasmic lambda light chains. By cytogenetic analysis and by blot hybridization of a highly polymorphic locus in human DNA, the tumor was of donor cell origin. Blot hybridization studies of tumor DNA demonstrated at least 70 per cent of the Epstein-Barr (EBV) genome at about 7 genome-equivalents per cell. The other tumor was an apparently isolated histiocytic lymphoma (large, noncleaved, follicular center cell lymphoma) resected from the lumbar epidural space 500 days following allografting of a 25-year-old male for myelofibrosis. The donor was his HLA-matched brother. Clinical acute GVHD had not been documented. The tumor was monoclonal and of host origin. These two cases differ in pretransplant diagnosis, development of clinical GVHD, tumor histology, and tumor genetic origin. (no Refs)

EPIDEMIOLOGY AND ETIOLOGY OF NON-HUMAN LEUKEMIA AND LYMPHOMA

7. REACTIVATION OF LATENT FELINE LEUKAEMIA VIRUS INFECTION.

Rojko JL, Hoover EA, Quackenbush SL, Olsen RG
Dept. Veterinary Pathobiology, Ohio State Univ., 484 W. 12th Ave., Columbus, OH, 43210
Nature; 298(5872):385-388 1982

Reactivation of latent feline leukemia virus (FeLV) from myelomonocytic and lymphoid cells of cats immune to FeLV, cats bearing FeLV-negative tumors, and kittens congenitally exposed to FeLV is reported. Self-limiting (regressive) FeLV infection was established in adult specific pathogen-free cats. At 16-20 wk after exposure, femoral bone marrow cells, mesenteric lymph node cells, peritoneal macrophages, and peripheral blood mononuclear leukocytes (PBML) were collected. High titers of FeLV were reactivated following isolation and in vitro propagation of marrow from 8/10 FeLV-immune cats, but not from four FeLV-naive cats. It was shown that refractoriness to retroviral replication accompanied differentiation of feline myelomonocytic progenitor cells. In samples from two cats with FeLV-negative lymphosarcoma of the lymph nodes, virus was reactivated only from cultured marrow cells, not blood or tumor cells. Two regressor females were mated with two regressor males and produced two litters of five kittens with evidence of congenital FeLV infections; both females had been re-exposed by a single ip dose of FeLV during the first wk of gestation. Infectious virus was expressed in cultured marrow from three kittens, cultured thymus of two kittens, and freshly isolated as well as cultured, liver hematopoietic cells from one fetal kitten. The in vitro and in vivo effect of corticosteroids on latent FeLV infections was studied; three of five cats contained reactivated FeLV, while two remained persistently viremic 135 days after initiation of treatment. Thus, FeLV persists as an integrated latent infection in marrow myelomonocytic precursor cells and T lymphocytes and can be reactivated by liberation from host immunological controls. (35 Refs)

8. THE GENETIC BASIS OF RETROVIRAL-INDUCED TRANSFORMATION.

Robinson HL, Vande Woude GF
Worcester Foundation Experimental Biology, 222 Maple Ave., Shrewsbury, MA, 01545
Curr Top Microbiol Immunol; 98:11-16 1982

The interaction of retroviruses with oncogenic sequences was studied in vitro and in vivo. In vitro studies with the Maloney sarcoma virus (MSV) indicated that the long terminal repeats (LTR) of MSV have transcriptional control sequences and structures that resemble insertion sequences. LTR enhanced transformation by an MSV DNA fragment containing the v-mos sequence (a viral homolog of the cellular c-mos sequence). Enhancement of transformation was accomplished either by directly linking the LTR and v-mos or by simultaneously transfecting a plasmid containing a single LTR with a plasmid containing v-mos. LTR may therefore enhance transformation by providing transcriptional control signals. LTR also activates transformation by c-mos. Transformation of cells by MSV apparently requires c-mos and LTR. Oncogenesis was studied in vivo by infecting K28 chickens with RAV-0 endogenous virus or with NTRE-7 (a nontransforming subgroup E recombinant of exogenous Pr-RSV-B and RAV-0 viruses). Of 58 chickens infected with RAV-0, none developed disease. Of 75 chickens infected with NTRE-7, 11 developed neoplasias (3 lymphomas, 2 fibrosarcomas, 2 carcinomas, 1 chondrosarcoma, and 3 osteopetroses). RAV-0 and NTRE-7 differ only in the immediate 3' sequences; therefore these sequences contain transcriptional controls for synthesis of viral messenger RNA that determine oncogenic potential in NTRE-7. Findings support a model of viral oncogenesis in which oncogenesis is controlled by the region of the viral genome that encodes control of transcription, and the type of neoplasia produced is determined by specific 3' oncogenic sequences. (16 Refs)

9. THE ONSET AND DEVELOPMENT OF MYELOID LEUKEMIA IN MALE MICE OF THE RF/J STRAIN: HEMATOLOGY, CLONING, AND PATHOLOGY.

McMorrow LE
New York University, New York, NY
Diss Abstr Int [B]; 42(7):2659-B 1982

Following whole-body irradiation (425R), male mice of the RF/J strain develop myeolid leukemia at a high incidence (48%) after a latency period of 5-6 months. The leukemia is characterized by a high white blood cell count (WBC), an increase in granulocytes in the peripheral blood, and frequently a decreased red blood cell count (RBC) and hematocrit. In the soft agar culture system, the proliferative capacity of bone marrow cells from leukemic animals is markedly suppressed as

compared to bone marrow cells from age-matched control animals. The time course of the leukemia is short: death follows in 3-4 weeks after detection of a high WBC count. No consistent deviation in either modal chromosome number or morphology has been found in direct bone marrow preparations. Tissue changes characteristic of leukemia are clearly evident in all leukemic animals. Spleen, liver, bone marrow and often thymus show involvement. Pathologic changes in those tissues can frequently be identified before clinical leukemia is evident. Myelocytic leukemia of the RF/J mouse is similar to the human disease in several respects. In both situations there is an increased high WBC count, a shift in the proportion of immature myelocytic cells in the peripheral blood smear, splenomegaly and hepatomegaly. Frequently, the developing leukemic, animal or human, shows a decreased WBC count just prior to the increase in WBC count. Leukemic individuals also frequently develop an anemia prior to or concomitant with the rise in WBC's. Bone marrow cells from leukemic RF/J mice fail to form colonies in the soft agar system, the pattern most frequently seen in human acute myelocytic leukemia. (no Refs)

10. BONE MARROW PROGENITOR CELLS OF AKR MICE GIVE RISE TO THYMIC LYMPHOMA CELLS.

Hays EF
Lab. Biomedical and Environmental Sciences, 900 Veteran Ave., Los Angeles, CA, 90024
Leuk Res; 6(3):429-432 1982

Twelve (AKR x DBA/2)F1 mice were given 400 rad and inoculated iv with bone marrow cells from 1-mo-old AKR donors. Six of the 12 mice developed thymic lymphoma between 158-244 days after cell inoculation and irradiation. Lymphoma occurred in three of nine control animals at 265, 280, and 287 days after irradiation. All of the six lymphomas occurring in mice given AKR bone marrow cells were thymic lymphomas. The microscopic morphology of the tumors as seen by hematoxylin and eosin prepared sections showed replacement of thymus, spleen, and lymph nodes by malignant lymphoblasts and infiltration of liver sinusoids and periportal areas with similar cells. One of the three control lymphomas was non-thymic. A retroperitoneal mass, slightly enlarged spleen, and no hepatomegaly were observed, and all lymph nodes were enlarged and replaced by tumor cells. The two remaining control lymphomas grossly resembled those of the experimental mice, but microscopic examination showed cells with pleomorphic nuclei and few mitoses. The microscopic findings in the control mice were in sharp contrast to the findings of large, round nuclei and abundant mitotic figures seen in the lymphomas from the AKR cell-treated mice. Four of the six experimental lymphomas were tested for growth in AKR mice. The lymphomas produced tumors 14-15 days after ip inoculation of 4 x 10(6) cells to AKR recipients. The findings implicate a bone marrow progenitor as a 'target cell' for the age-related development of thymic lymphomas in AKR mice. (7 Refs)

CYTOGENETIC AND MORPHOLOGIC STUDIES

11. NEAR-HAPLOID CHROMOSOME NUMBERS IN LEUKEMIA: SIGNIFICANCE TO LEUKEMOGENESIS (MEETING ABSTRACT).

Chaganti RS
Laboratory of Cancer Genetics and Cytogenetics, Memorial-Sloan-Kettering, Cancer Center New York, NY, 10021
Am J Hum Gen; 33(6):61A 1982

Chromosome numbers in most leukemias, when abnormal, cluster around either the diploid (hypo or hyper) or tetraploid (hypo to hyper) modes arising through non-disjunction and endoreduplication. Marker chromosomes also often characterize leukemic cells. Extremely rare instances of severe hypodiploidy have been reported in acute lymphoblastic leukemia (ALL) and in blastic phase chronic myelogenous leukemia. We report three cases of ALL with near haploid chromosome numbers. These along with three other cases reported in the literature comprise a new cytogenetic entity among ALL. Our patients number 1 and 2 were 7-year-old and 18-year-old males, while patient number 3 was a 16-year-old male. The leukemic marrow clones of the three patients exhibited 24, 26, and 28 chromosomes, respectively. In each case, a complete haploid set of autosomes and both sex chromosomes were present. In addition, chromosomes number 14 and 21 in the case of patient number 2 and chromosomes number 6, 10 and 21 in the case of patient number 3 were present in two copies. Rearrangements were absent. This cytogenetic picture suggests derivation by either non-disjunction and chromosome elimination or by a form of reductional division restricted to autosomes with subsequent restoration of disomy of some chromosomes through non-disjunction. (no Refs)

12. SIGNIFICANCE OF A (4;11) TRANSLOCATION IN ACUTE LYMPHOBLASTIC LEUKEMIA.

Esseltine DW, Vekemans M, Seemayer T, Reece E, Gordon J, Whitehead VM
Service of Hematology, Montreal Children's Hosp., 2300 Tupper St., Montreal, Quebec H3H 1P3, Canada
Cancer; 50(3):503-506 1982

This report describes a case of null cell congenital acute lymphoblastic leukemia associated with a (4;11) translocation that may be specific for congenital acute lymphoblastic leukemia. This chromosome abnormality is commonly associated with acute lymphoblastic leukemia and probably more specifically with congenital acute lymphoblastic leukemia. A review of the literature is presented. (32 Refs)

13. CHROMOSOMAL FINDINGS AND THEIR CORRELATION TO PROGNOSIS IN ACUTE LYMPHOCYTIC LEUKEMIA.

Kaneko Y, Hayashi Y, Sakurai M
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Cancer Genet Cytogenet; 4(3):227-235 1981

Sixteen of the 17 patients with acute lymphocytic leukemia (ALL) were revealed to have chromosome abnormalities in their leukemic cells. Of nine children, six had modal chromosome numbers between 50 and 59; these patients and one additional patient with a pseudodiploid karyotype have achieved and retained a complete remission. The only patient without chromosome abnormalities achieved a remission, but had a re-

lapse and died. The only child who expired without achieving a remission had 47 chromosomes in his leukemic cells. Of eight adults, none had the hyperdiploidy seen in the children. The four with hypo- or pseudodiploidy failed to achieve a complete remission. One patient had 47 chromosomes in his leukemic cells, and this patient and the remaining three, all with ploidy abnormalities, achieved a complete remission, but a relapse occurred and they died. The chromosomal abnormalities were very extensive in most cases, many patients having marker chromosomes of an unknown origin. Four patients clearly exhibited karyotypic evolution when they relapsed. The patients with hyperdiploidy had a better prognosis, and those with pseudodiploidy had a poorer prognosis. The role of individual chromosome aberrations, however, remains to be elucidated. (Author abstract) (27 Refs)

14. CHROMOSOME ABNORMALITIES IN JAPANESE BURKITT LYMPHOMA CELL LINES.

Hamasaki K
Second Dept. Internal Medicine, Okayama Univ. Medical Sch., Okayama 700, Japan
Acta Med Okayama; 36(1):23-38 1982

Six established Japanese Burkitt lymphoma (BL) cell lines including one case with null cell type were studied by chromosomal banding techniques. The modal chromosome number was diploid or nearly diploid in five cases and hyperdiploid in one case. The marker chromosome 14q+ was observed in four of the six cases; the origin of the extra band was a chromosome 8 in three including the null cell case but could not be identified in the other. The two cases lacking the 14q+ marker had variant translocations involving the long arm of chromosome 8, one of which carried a translocation, t(8;22) (q24;q13) and the other a translocation, t(2;8) (p12;q24). Although structural and/or numerical aberrations were found in all six cell lines, chromosome 8 was the one most consistently involved. This frequent involvement of chromosome 8 in aberrations, therefore, may be an important event in the development of BL rather than the presence of a 14q+ marker chromosome. (Author abstract) (44 Refs)

15. PLACE OF CENTROCYTOMA AND CENTROBLASTOMA WITHIN THE CLASS OF MALIGNANT LYMPHOMAS.

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Cesk Patol; 18(2):81-89 1982

The interrelationships between the tumor cells were studied in 33 multiparametrically verified lymphomas of centrocytic and centroblastic origin (centrocytomas, centroblastic-centrocytic lymphomas and centroblastomas). The ratio of centrocytes to centroblasts was found to be independent in many respects, being mostly topical. The centrocytomas regularly showed a tendency to produce a follicular type of organization manifesting itself in a definite polarity even in the cytologically pure variants. However, the polarity of the follicular structures was due to the transition of the small cohesive centrocytes into large centrocytes lacking cohesion. The polar follicular organization is probably based on the transition of the small centrocytes into the large ones. The extracellular regions of the follicular centrocytoma are usually formed by second-generation lymphocytes with cleaved nuclei, the leukemic transformation of which is usually the expression of an 'atypical chronic lymphocytic leukemia' (CLL). Not even the nodular variants of centroblastoma showed any trully follicular configuration. The ratio of centroblasts to centrocytes was less constant than that to immunoblasts and lymphoplasmoid cells, which were close to the typical CLL in the case of leukemic transformation. The centroblast as a whole appears to be an element more or less 'cooperating' with the centrocytes, while being independent otherwise, without any direct or obligatory participation in the succession of the blast transformation of the B lymphocytes. (6 Refs) (In CZE)

BIOCHEMICAL, IMMUNOLOGICAL AND OTHER CELL BIOLOGY STUDIES

16. GENERATION OF LONG-TERM T-LYMPHOID CELL LINES WITH SPECIFIC CYTOTOXIC REACTIVITY FOR A SYNGENEIC MURINE LYMPHOMA.

Eberlein TJ, Rosenstein M, Spiess PJ, Rosenberg SA
NIH, Building 10, Room 10N 116, Bethesda, MD, 20205
JNCI; 69(1):109-116 1982

The long-term in vitro growth in T-cell growth factor (TCGF) of murine cytotoxic T-lymphoid cells directed against syngeneic tumor antigens was investigated. C57BL/6 mice were immunized to syngeneic FBL-3 lymphoma by two ip injections of irradiated FBL-3 lymphoma cells. Splenocytes from these animals were injected into mice with disseminated lethal FLB-3 tumor. The injection of cyclophosphamide (Cy) plus immunized lymphocytes significantly improved survival with cure of 53% of 38 animals. In comparison, treatment with Cy alone resulted in 0 to 31 cured and treatment with Cy plus unimmunized cells resulted in 0 of 40 cured (p less than 0.0005). These in vivo immunized lymphocytes were reexposed to FBL-3 tumor in vitro for 5 days in lectin-free TCGF (LF-TCGF). Although in vivo and in vitro sensitized lymphocytes exhibited no cytotoxicity toward fresh FBL-3 tumor cells in an 18-hour 51Cr release assay, expansion of appropriately sensitized cells in LF-TCGF resulted in significant lysis of fresh FBL-3 tumor cells. This significant lysis was specific and lysed syngeneic FBL-3 but not syngeneic MCA-103 fresh tumor targets. This maximal specific cytotoxicity was maintained for 2.5 months. A screening assay was developed that permitted rapid identification and isolation of low-frequency cytotoxic clones with reactivity specific for FBL-3 tumor. Several of these cloned cells were grown for almost 3 months with maintenance of high degrees of specific lysis (as much as 4,500 lytic U/10(6) cells). These cytotoxic lines and clones will be of value for the study of tumor-host immunologic interactions and perhaps for use in adoptive immunotherapy. (Author abstract) (68 Refs)

17. ESTABLISHMENT OF FUNCTIONAL, ANTIGEN-SPECIFIC T CELL LINES BY RADLV-INDUCED TRANSFORMATION OF MURINE T LYMPHOCYTES.

Ricciardi-Castagnoli P, Rabbiati F, Barbianti E, Doria G, Adorini L
No affiliation given
Curr Top Microbiol Immunol; 100:89-96 1982

Radiation leukemia viruses (RadLV) were produced by exposing C57Bl/Ka mice to radiation. The RadLv were isolated from the resulting thymomas. T-cell lines containing the viruses were established that secrete antigen-specific and maintain functional activity in spite of undergoing transformation. RadLV in the T-cell lines are endogenous leukemogenic retroviruses with high oncogenic capacity. RadLV induce neoplas-

tic transformation in target tissues including bone marrow, spleen, thymus, and fetal liver. No transformation of cells of B lineage has not been reported. Antigen-specific T lymphocytes can be infected with RadLV in vitro; transformation occure, however, only if the cells are maintained under conditions which support cellular proliferation. Cells bearing the H-2b haplotype or the Fv-1bb gene are the most susceptible to infection with RadLV; other cell types tend to be resistant to RadLV. Antigen-specific, functional T-cell lines are established by enriching specific T-cells and then infecting them with RadLV. The infected cells are then injected into sublethally irradiated mice, and tumors are allowed to develop. Individual cell lines are produced by cloning. Cells are selected for cloning by means of phenotypic and functional assays. Products of a T-cell line specific for hen egg-white lysozyme (HEL) have been characterized. Since the HEL-specific cells do not suppress a structurally related lysozyme, the specificity of the cells is quite narrow. The specificity is determined by the N-terminal, C-terminal peptide in the HEL molecule. Suppressor activity is restricted by genes located in the H-2 complex and requires identity of the I-J region of the H-2 complexes of the cell factor and its target. (16 Refs)

18. T LYMPHOCYTE-MEDIATED SUPPRESSION OF TUMOR GROWTH IN MICE WITH FRIEND LEUKEMIA VIRUS DORMANT INFECTIONS (MEETING ABSTRACT).

DiCicco LM, Truitt GA, Fuscaldo KE, Wheelock EF
Department of Pathology, Hahnemann Medical College, Philadelphia, PA, 19102
Proc Am Assoc Cancer Res; 23:1095 1982

DBA/2 mice can be immunostimulated to suppress a leukemogenic dose of Friend virus (FLV) to a dormant state for many months. Intravenous inoculation of FLC-745 cells (FLV-transformed erythroleukemic cells) into normal DBA/2 mice resulted in FLV-induced splenomegaly, tumor cell proliferation in the spleen and death with 20 days. Mice with FLV-dormant infections resisted all of these sequelae. Nevertheless, many FLV-dormant mice contained small numbers of tumor cells in their spleen several months after FLC-745 cell inoculation. These tumor cells were distinguished from the original FLC-745 cell inoculum by reduced levels of cell surface H-2 and gp 70. However, they were induced with DMSO (dimethylsulfoxide) to produce hemoglobin, thereby suggesting a progeny relationship with the FLC-745 cells. To investigate the mechanisms involved in resistance of FLV-dormant mice to tumor cell proliferation and in the maintenance of the FLV-dormant state we used a subcutaneous Winn assay in normal mice which had been given 450 X-irradiation. FLV-dormant spleen cells admixed with FLC-745 cells suppressed the tumor nodule formation which resulted from inoculation of FLC-745 cells either alone or admixed with normal spleen cells. Suppression of FLC-745 tumor growth was specific since FLV-dormant spleen cells did not suppress L5178Y cell tumor growth. The FLV-dormant splenic effector cells bear the Thy 1.2 surface marker, are sensitive to 1000 R x-irradiation and do not adhere to fetal calf serum-coated plates. (no Refs)

19. CHARACTERIZATION OF THE NATURAL KILLER (NK) TARGET CELL POPULATION IN PRELEUKEMIC C57BL/6 MICE (MEETING ABSTRACT).

Munson D, Waksal SD, Parkinson DR
Departments of Medicine and Pathology, Tufts Cancer Research Center, Boston, MA, 02111
Fed Proc; 41(3):601 1982

Alterations in preleukemic cell populations were studied in the C57Bl/6 split-dose irradiation-induced model of thymic leukemia. We have previously shown NK cell activity to be depressed shortly after completion of the leukemogenic irradiation protocol. This is associated with the appearance of cells in the bone marrow and spleen of irradiated mice which are capable of blocking NK cell lysis of YAC-1 tumor targets. This blocking cell population is contained within the peanut agglutinin (PNA) positive cell fraction in both bone marrow and spleen. Studies using fluorescence activated cell sorter (FACS) have demonstrated cells expressing murine leukemia antigens (MuLV) in the bone marrow, spleen and thymus of irradiated mice at various time points following irradiation. During the same period, a large cell population is detectable initially in bone marrow and spleen and subsequently in thymus of irradiated mice. The present study characterizes the PNA positive, NK blocking cell population found in split-dose irradiated mice with respect to cell size, viral antigen expression and sensitivity to NK cell mediated cytolysis. (no Refs)

20. NATURAL CYTOTOXICITY IN AKR/J MICE DURING ADJUVANT INDUCED AMYLOIDOGENESIS.

Fuhrman SA, Parkinson DR, Waksal SD, McAdam KP
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Cell Immunol; 70(1):170-179 1982

The induction of amyloidosis in AKR mice has previously been shown to be associated with a decrease in the incidence of spontaneous thymic leukemia. Amyloid induction with azocasein depresses the activity of the natural killer (NK) cell, a cell believed to be important in the protection against the development of malignancy. In the present studies, therefore, we examined the response of the NK cell to the induction of amyloidosis in AKR mice. Rapid and long-term depression of NK cell activity against YAC-1 tumor cells was noted following intraperitoneal administration of complete Freund's adjuvant enriched with Mycobacterium butyricum. Mixing studies suggested that active suppression did not account for the observed decrease in NK cell activity. Although some NK cell activity was noted in ascitic fluid, redirection was not felt to account for the rapid and dramatic reduction in splenic NK cell activity. Furthermore, serum from adjuvant-treated but not control mice was found to significantly inhibit NK cell activity in vitro. These studies therefore suggested a role for a serum factor in the depression of this activity. The apparent paradox of decreased NK cell activity in a setting of diminished leukemogenesis is considered in relation to previous studies describing impaired T-cell functioning after the induction of amyloidosis. (Author abstract) (43 Refs)

21. NON-IMMUNOGLOBULIN-ASSOCIATED DNA REARRANGEMENTS IN MOUSE PLASMACYTOMAS.

Harris LJ, Lang RB, Marcu KB
(c/o Marcu) Biochemistry Dept., State Univ. New York at Stony Brook, Stony Brook, NY, 11794
Proc Natl Acad Sci USA; 79(13):4175-4179 1982

We have characterized a class of DNA rearrangements in plasmacytomas. These recombination events involve a DNA sequence whose origin is outside of the locus of the heavy chain constant region genes, CH. Therefore, we choose to refer to this sequence as non-immunoglobulin-associated rearranging DNA (NIARD). We have isolated two abortively rearranged C alpha genes, generated by NIARD events from the alpha-producing J558 myeloma. Restriction endonuclease maps of these sequences reveal two possible recombination sites in NIARD that are separated by approx 6.5 kilobase pairs of

DNA (defined at 5' and 3' sites). A NIARD rearrangement occurs in 15 out of 20 plasmacytomas tested, including gamma3-, gamma1, gamma2b-, gamma2a-, and alpha-producers, but this event usually does not involve a CH switch (S) region. In fact, only S alpha appears to accept NIARD. However, NIARD did not undergo a rearrangement in eight IgA-producing hybridomas tested. One germ-line copy of NIARD (a 22-kilobase pair EcoRI fragment) is retained in all plasmacytomas. NIARD does not appear to possess repetitive DNA sequences homologous to S mu or S alpha. We discuss the possible role and implications of NIARD-like sequence rearrangements in allelic exclusion and chromosomal translocation events in plasmacytomas. (Author abstract) (30 Refs)

22. STUDIES OF THE PLASMA MEMBRANE IN THE DIFFERENTIATION OF NORMAL AND MALIGNANT THYMOCYTES.

Casteel N
University of Health Sciences/The Chicago Medical School, Chicago, IL
Diss Abstr Int [B]; 42(10):4009-B 1982

The role of the plasma membrane in the differentiation and activation of thymocytes and how cyclic nucleotide-related enzymes are altered with the progress of leukemia was investigated. Enzyme levels of thymocytes of normal, preleukemic and leukemic mice were compared. Both virally-induced leukemia of AKR mice and chemically-induced leukemias of Swiss mice injected with 5-(3,3-dimethyl-1-triazeno)imidazole-4-carboxamide (DTIC) were studied. While total AMPase activity appeared erratic, 5'-nucleotidase dropped significantly while alkaline phosphatase activity rose dramatically in the thymocytes of both leukemic models. Preleukemic thymocytes showed intermediate values. This is in contrast to normal developmental changes, where the activities of 5'-nucleotidase and alkaline phosphatase rise in parallel. Phosphodiesterase activity of the thymocytes of these mice also became elevated with leukemia, confirming that the enzymic changes that would lead to lowered cAMP levels and increased proliferation, ie, lowered 5'-nucleotidase and elevated phosphodiesterase activities are controlling factors in the development of both virally-induced and chemically-induced leukemias. (no Refs)

23. CIRCULATING IMMUNE COMPLEXES, ANTIGENS, AND ANTIBODIES RELATED TO THE MURINE MAMMARY TUMOR VIRUS IN C3H MICE.

Dong ZW, Witkin SS, Fernandes G, Sarkar NH, Good RA, Day NK (c/o Day), Oklahoma Medical Res. Foundation, 825 N.E. 13th St., Oklahoma City, OK, 73104
J Immunol; 129(2):872-876 1982

A comparative study was performed to measure levels of free antibody to MuMTV, MuMTV membrane antigen (gp52), and antigen-antibody complexes in sera of mammary tumor-bearing and age-matched non-tumor bearing C3H/Bi mice. Approx 90% of these mice spontaneously develop breast cancer. Levels of MuMTV antibody and C3-containing circulating immune complexes (CIC) were highest in the sera of the mice without overt evidence of breast cancer. MuMTV gp52 antigen was present in higher concentrations in the sera of mice with overt breast cancer. Fractionation of the sera on sucrose gradients followed by analysis for CIC confirmed that levels of C-containing CIC were lower in sera from mice with tumors than in nontumor bearers. The CIC were, however, of smaller size in sera of tumor-bearing mice. When the sera were assayed for CIC by an assay in which C binding does not compete with binding of CIC to the sperm, the levels of these small-sized CIC in sera of mice with breast cancer were now comparable to CIC levels in nontumor-bearing mice. MuMTV antibody was located in both 7S and high mw regions of the gradients. To determine whether the CIC contained MuMTV antigen, the CIC were bound to bull sperm Fc receptors and assayed for reactivity with monospecific goat anti-gp521gG. Significantly higher levels of reactivity to anti-gp52 were detected in CIC from C3H mice than in CIC from sera of age-matched AKR mice with or without leukemia or from MRL/MpJ-lpr/lpr mice. These data indicate that there is a shift from MuMTV antibody excess to MuMTV antigen excess and from larger C-fixing CIC to smaller non-C-fixing CIC after appearance of overt breast cancer in C3H mice. (26 Refs)

24. SURFACE ANTIGEN EXPRESSED IN HEMATOPOIETIC CELLS DERIVED FROM FV-4 MOUSE STRAINS.

Yoshikura H, Odaka T
Dept. Microbiology, Univ. Tokyo, P. O. Box Hongo, Tokyo 113, Japan
JNCI; 68(6):1005-1009 1982

Fv-4 locus controls the susceptibility of mice to ecotropic murine leukemia virus. Antiserum against Fv-4r/s mice with BALB/c background was raised in inbred BALB/c mice. In the complement-dependent cytotoxicity test, the antiserum killed the hematopoietic cells derived from Fv-4r/- mice but not those from Fv-4s/s mice, and the genetic cross experiments located the locus controlling the expression of the target molecule of the antibody in the close vicinity of Fv-4. In addition, the antigenic expression of the exogenously infecting MuLV suppressed the expression of the target molecule of the antiserum. The expressions of these two antigens appear to compete with each other on the cell surface. (Author abstract) (21 Refs)

25. STUDIES ON THE CLONAL ORIGIN OF HUMAN B CELL LEUKEMIA USING MONOCLONAL ANTI-IDIOTYPE ANTIBODIES.

Mayumi M, Kubagawa H, Omura GA, Gathings WE, Kearney JF, Cooper MD
224 Tumor Inst., Univ. Alabama in Birmingham, University Station, Birmingham, AL, 35294
J Immunol; 129(2):904-910 1982

The clonal origin of an IgA1kappa B cell leukemia in a 71-yr-old man (WF) was examined using a monoclonal anti-Id antibody and a panel of monoclonal anti-VH antibodies. Immunofluorescent studies revealed that all surface IgA1kappa+ leukemic cells in WF's blood and 10% of the IgM+ B cells in his bone marrow expressed the WF Id. Three percent of the IgA1kappa+ leukemic cells in blood also expressed gamma-chains in their cytoplasm. Approximately 0.1%, 1%, and 10% of bone marrow mononuclear cells, respectively, expressed u-chains, gamma-chains, and alpha-chains in their cytoplasm, but no detectable light chains or surface immunoglobulins. These u-, gamma-, and alpha-positive cells had the convoluted nucleus and narrow cytoplasm characteristic of normal u+ pre-B cells. Sequential isotype switching among this unusual pre-B population was indicated by co-expression of u-chains and alpha-chains by 11% and 63%, respectively, of the gamma pre-B cells. These pre-B cells and the surface alpha-chains and cytoplasmic gamma-chains of the leukemic B cells were reactive with one of four monoclonal anti-VH antibodies. The data suggest malignant transformation of the clone before isotype

switching, and also imply light chain precommitment at the pre-B cell level of differentiation. (Author abstract) (35 Refs)

26. TDT-POSITIVE AND TDT-NEGATIVE HUMAN LEUKEMIC CELLS: SPECIFIC DENSITY AND MORPHOLOGY.

Marini M, Bagnara GP, Biagini G, Baccarani M, Rosito P
Istituto di Istologia ed Embriologia Generale, Facolta di Medicina, 401000 Bologna, Italy
Adv Exp Med Biol; 145:367-370 1982

Cell density distribution of normal terminal deoxynucleotidyl transferase (TdT) positive bone marrow cells was compared with that of TdT positive leukemic blast cells to study the nature of the leukemic populations. Ultrastructural features of cell fractions expressing or not expressing the marker in the different leukemias were examined. In 10 untreated patients with Philadelphia chromosome (Ph1) positive chronic myeloid leukemia (CML) studied at the onset of the disease, no TdT activity was observed. One of the patients underwent a TdT positive blastic crisis 8 mo later, suggesting that TdT positive cells arise, at least in a sizable number at the onset of the blastic crisis and then accumulate rapidly. TdT was evaluated in 31 patients during the blastic crisis of CML and in 3 patients undergoing the blastic transformation following other myeloproliferative disorders. Fourteen CML-blastic crisis TdT positive cells were found in 14 CML-blastic crisis patients, the involved lymph nodes in one additional patient, and in the lymph nodes of a patient with agnogenic myeloid metaplasia in blastic proliferation. Three TdT positive and two TdT negative patients were Ph1 negative. No correlation between TdT-positivity and length of chronic phase was observed. A total of 67 patients with acute lymphoid leukemia were studied during a 3-yr period. Nine of 10 TdT negative adult patients had very low peripheral blast cell counts (less than 500/ul), which might have been caused by the insensitivity of the assay for very small numbers of TdT positive cells. (17 Refs)

27. PURIFICATION AND CHARACTERIZATION OF MULTIPLE FORMS OF TERMINAL TRANSFERASE FROM HUMAN LEUKEMIC CELLS.

Deibel MR, Coleman MS, Hutton JJ
Dept. Biochemistry, Univ. Kentucky, Lexington, KY
Adv Exp Med Biol; 145:37-60 1982

Biochemical properties of human terminal transferase (TdT) were analyzed in human lymphoblasts derived from therapeutic leukapheresis. Isolation of the purified enzyme demonstrated that, regardless of the source or mol wt, the protein is catalytically active and appears to be homogeneous in structure. Determination of the kinetic mechanism provided a model system for the comparable, yet far more complex eucaryotic DNA polymerases. The reaction catalyzed by human TdT followed a rapid equilibrium random mechanism as determined by initial velocity and product inhibition studies with oligodeoxyadenylate initiators. (15 Refs)

28. BASOPHIL PRODUCTION IN MYELOPROLIFERATIVE DISORDERS: INCREASES DURING ACUTE BLASTIC TRANSFORMATION OF CHRONIC MYELOID LEUKEMIA.

Denburg JA, Wilson WE, Bienenstock J
Dept. Medicine and Pathology, McMaster Univ. Health Sciences Center, Hamilton, Ontario 18N 325, Canada
Blood; 60(1):113-120 1982

We have examined basophil production (BP) in suspension cultures of separated peripheral blood cells from patients with chronic myeloid leukemia (CML). Seventy cultures were performed in 47 patients, 33 in chronic and 14 in the accelerated/acute phase of CML. None of 13 normal controls, 0/21 treated chronic phase, 3/33 untreated chronic phase, and 14/18 (p less than 0.0001) accelerated/acute phase CML cultures showed at least twofold increases in basophils and histamine in vitro at 14-21 days. A gradient effect of disease phase on BP was observed: maximal histamine content (ng/10(6) cells) was 16 +-4 for chronic, 56 +-19 for accelerated, and 183 +-73 for acute phase CML cultures (mean +- SE, p less than 0.002), while basophils (per 10(3) cells) numbered 23 +-7, 59 +-20 and 267 +-81, (mean +- SE, p less than 0.0003), respectively. Multivariate analysis of maximal differences in basophils or histamine in vitro and simple linear regression slopes of basophils or histamine on time revealed that disease phase, and not therapy, accounted for the changes in BP in vitro. Serial studies over periods of 6-29 mo in four patients followed from chronic through acute phases of disease revealed a reversal of BP in vitro from negative to positive in four/four, with death supervening within 3 mo of study in three cases and refractory leukemia developing in the other. Whole blood histamine values were highest in untreated chronic phase CML (1,599 +-306 ng/ml, mean +- SE), while accelerated/acute phase values were comparable to treated chronic phase (513 +-131 and 521 +-101 ng/ml, respectively). Whole blood histamine and BP in CML relate closely to impending acute blastic transformation. The potential role of basophils and histamine in myelopoiesis and acute leukemic transformation of CML is discussed. (Author abstract) (26 Refs)

EXPERIMENTAL STUDIES INVOLVING CHEMICAL AGENTS AND IRRADIATION

29. DNA-REPAIR SYNTHESIS IN BLAST CELLS FROM PATIENTS WITH ACUTE MYELOBLASTIC LEUKAEMIA.

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Scand J Haematol; 28(5):399-407 1982

DNA-repair synthesis was studied in blast cells from patients with acute myeloblastic leukemia. The DNA-repair synthesis, measured as 3H-thymidine incorporation, was registered as unscheduled DNA synthesis by autoradiography, and also after suppression of the replicative DNA synthesis by hydroxyurea by liquid scintillation. There was good correlation when results from both methods were compared. A significantly wider variation of unscheduled DNA synthesis was found in leukemic as compared to normal blast cell populations. There was also a wider variation within individual leukemic blast cell samples compared to normal samples. A correlation was found between unscheduled DNA synthesis induced by nitrogen mustard and by UV-irradiation in the leukemic blast cell populations. The UV-induced unscheduled DNA synthesis in some of the leukemic blast cell populations continued to increase at doses of UV-irradiation at which normal myeloblasts had reached their max level of unscheduled DNA synthesis. This indicates that at least some malignant blast cell populations may possess an effective DNA-repair system. (Author abstract) (21 Refs)

30. LYMPHOCYTES FROM CHRONIC LYMPHOCYTIC LEUKEMIA PATIENTS: ABILITY OF EXTRACTS TO REMOVE O6METHYLGUANINE FROM ALKYLATED DNA (MEETING ABSTRACT).

Setlow RB, Waldstein EA, Cao EH, Miller ME, Cronkite EP
Biology and Medical Departments, Brookhaven National Laboratory, Upton, NY, 11973
Proc Am Assoc Cancer Res; 23:51 1982

O6methylguanine (O6MeGua) is a presumptive mutagenic and carcinogenic product in DNA treated in vivo or in vitro with N-nitroso compounds. Normal human cell lines (mer+) remove 6MeGua from their DNA whereas an appreciable number of tumor and virus transformed cell lines are deficient (mer-) in this respect. We examined the O6MeGua-removing capacity of lymphocytes from 6 patients with chronic lymphocytic leukemia (CLL) and one with polycythemia vera (PV). Unexpectedly lymphocytes from CLL patients, mainly B type, appeared to be super mer+, showing an increased capacity to remove O6MeGua when compared to B type lymphocytes of normal individuals. The activity per cell increases with the WBC and the stage of the disease. Unlike normal lymphocytes, incubation of lymphocytes from CLL patients with or without phytohemagglutinin results in a decrease rather than an increase in activity. The activity from CLL patients, as in normal lymphocytes, acts in a stoichiometric fashion and transfers about 80% of the methyl groups to a cysteine moiety of an acceptor protein. The number of acceptor molecules per cell in lymphocytes of CLL patients is estimated to range between 94,000 and 240,000-4 to 10 fold higher than in normal B type lymphocytes. The estimate for lymphocytes from PV patients is about 40,000 which falls in the range of 14,000-110,000 per cell estimated for unstimulated lymphocytes, mostly T type, of normal individuals. (2 Refs)

31. ARYL HYDROCARBON HYDROXYLASE (AHH) INDUCIBILITY AMONG PRIMARY RELATIVES OF CHILDREN WITH LEUKEMIA OR SOLID TUMORS (MEETING ABSTRACT).

Levine AS, McKinney CE, Echelberger C, Kouri RE, Edwards BK, Nebert DW
National Cancer Institute, Bethesda, MD, 20205
Proc Am Assoc Cancer Res; 23:191 1982

Polycyclic aromatic-inducible AHH activity in 'Ah-responsive' (Ahb) mice is highly inducible by many polycyclic aromatic compounds; the activity in 'Ah-nonresponsive' (Ahd) mice is 12-18 x less inducible. Compared with Ahd mice, Ahb mice develop more tumors at the site (topical, subcutaneous, or intrapulmonary) of administered procarcinogen. Compared with Ahb mice, Ahd mice develop more leukemia when polycyclic hydrocarbons are given topically or in the diet. In adult cancer patients, previous studies have been contractory with regard to an association between AHH inducibility and lung cancer. In the only report of children with acute leukemia, low AHH inducibility was found in the patients themselves. In the present study, AHH inducibility was examined in mitogen-stimulated cultured lymphocytes from parents and siblings of children with leukemia or solid tumors. Control families (parents and children but no one with cancer) comprised friends or neighbors of the proband families. Adjusting for age, smoking history, and length of time the lymphocytes were frozen, we found no difference among 104 control, 80 acute leukemia, and 73 solid tumor family members with regard to median maximally induced AHH activity/cytochrome c reductase activity: 0.92+/-0.24, 0.96+/-0.15, and 0.98+/-0.58, respectively. (no Refs)

32. A CONTRIBUTION TO THE INVESTIGATION OF TARGET CELLS IN N-NITROSO-N-METHYL UREA-INDUCED LEUKEMOGENESIS IN MICE.

Seidel G
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Arch Geschwulstforsch; 52(6):451-458 1982

Chemical leukemogenesis by administration of N-nitroso-N-methyl urea (NMU) was studied in (XVII x AKR)F1 rats to determine the target organ and target cells of the carcinogen. NMU was labeled with NMU (0.1 mg/g body wt) was injected ip or sc into rats of various ages. NMU was administered in a single dose or in two fractions at an interval of 4 wk. Rats were killed at 5 hr, 1, 2, 4, and 15 days after injection of the labeled NMU. Blood, lungs, liver, spleen, kidney, lymph nodes, thymus, bone marrow, and brain tissue were examined for MNU content by scintillation counting and autoradiography. The DNA content of thymus, bone marrow, lymph nodes, and spleen ranged from 8,200 to 9700 ug/g tissue. Labeled NMU reached the highest concentrations in the bone marrow. Significant amounts (5,500 disintegrations/mg: dpm/mg bone marrow) of NMU were found 5 hr after injection. The lowest amounts were found in the blood and brain (150 dpm/mg). Values for lung, liver, spleen, kidney, lymph node, and thymus tissue were 300-1,200 dpm/mg. Since DNA synthesis was approx equal in bone marrow, thymus, and lymph node tissue, the increased labeling of bone marrow with NMU was specific for bone marrow. The bone marrow is evidently the target organ for leukemogenesis by NMU. Lymphatic cells in the marrow are probably the target cells. The thymus apparently is not essential for lymphatic leukemogenesis. (37 Refs) (In GER)

33. RADIOBIOLOGICAL EQUIVALENT OF BENZO(A)PYRENE CARCINOGENICITY DURING INHALATION EXPOSURE.

Knizhnikov VA, Grozovskaia VA, Barkhudarov RM, Novikova NIa, Bugrova NV
No affiliation given
Gig Sanit; (7):23-27 1982

To evaluate the radiobiological equivalent of benzo(a)pyrene (BP) carcinogenicity, random-bred female albino mice were subjected to inhalation exposure to BP aerosol (6 hr/day, 5x/wk, for 3 mo). BP concentration in exposure chambers was 0.2 (Group 1), 6.3 (Group 2) and 78 ug/cubic meter (Group 3). The animals were followed-up until their natural death. Av concentration of BP in the lung tissue in the animals from Group 1, 2, and 3 was 0.025, 0.8, and 9.0 ug/g, respectively. The mice subjected to inhalation exposure to BP developed lung carcinomas, lymphosarcomas, and adenocarcinomas. The histology of BP-induced lung tumors was identical to that of human lung cancer. These findings indicate that the yield of BP-induced lung tumors can be approximated by the exponential curve, and that the carcinogenicity of BP after inhalation exposure was significantly greater than that after other methods of intratracheal administration. (16 Refs) (In RUS)

34. EVALUATION OF POTENTIAL CARCINOGENICITY OF CIODRINE.

Didenko GG, Gupalovich TD, Petrovskaia OG
All-Union Res. Inst. Hygiene and Toxicology, Pesticides,, Polymers, and Plastics Kiev, USSR
Gig Sanit; (7):83-84 1982

Potential carcinogenicity of acaricide ciodrine (O,O-dimethyl-O,1-methyl-2 (phenylcarbethoxy)vinylphosphate) was

studied in random-bred mice and rats. The animals were subjected to intragastric administration of ciodrine (6 mg/kg in mice and 10.7 mg/kg in rats, 2x/wk, for 18 wk). Duration of the experiment was 72 wk (mice) or 78 wk (rats). The incidence of ciodrine-induced tumors in mice was 16.5% (23.9% in females and 10.3% in males), compared with 20.9% in non-treated controls. The incidence of ciodrine-induced tumors in rats was 8.1% (7% in females and 9.2% in males), compared with 9.6% in controls. Both ciodrine-treated and control mice and rats developed benign and malignant tumors of the lung, mammary gland, and hematopoietic organs. This experiment failed to demonstrate the carcinogenic activity of ciodrine. (3 Refs) (In RUS)

35. THE INDUCTION OF THE D-T DIAPHORASE AND THE NAD(P)H-NITRO BT REDUCTASE BY CARCINOGENIC POLYCYCLIC HYDROCARBONS IN THE SPLEEN AND LYMPH NODES OF THE RAT (MEETING ABSTRACT).

Schor NA
Department of Pathology, Tulane University School of Medicine, New Orleans, LA, 70112
Fed Proc; 41(3):330 1982

The polycyclic hydrocarbons 3,4-benzpyrene, 7,12-dimethylbenzanthracene and 3-methyl cholanthrene induce the activity of the soluble enzyme D-T diaphorase in rat spleen and lymph nodes. The dehydrogenation of NAD(P)H in fractions sedimented at 8000 and 100000 g in the same animals is not affected by the treatment. The induction of the soluble diaphorase is dose dependent and is inhibited by dicumarol. The histochemical activity of the NAD(P)H-NBT reductase is also induced by carcinogens, this enzyme is localized in histiocytes and T lymphocytes; B lymphocytes, even after the administration of carcinogens, show a very weak activity. The staining of the NAD(P)H-NBT reductase is not specific for the D-T diaphorase but the negative effects of the carcinogens on the particulate enzymes suggest the observed increase in histochemical activity may be due to the D-T diaphorase. These results seem to indicate that a) lymphoid organs participate actively in the metabolism of carcinogens, b) this function may be specific for histiocytes and T lymphocytes, and c) the inductive histochemical and biochemical action of carcinogens may be another useful and reliable parameter to differentiate B and T lymphocytes in experimental animals. (no Refs)

EXPERIMENTAL STUDIES: RNA TUMOR VIRUSES

36. THYMIC EPITHELIUM IS PROGRAMMED TO INDUCE PRELEUKEMIC CHANGES IN RETROVIRUS EXPRESSION AND THYMOCYTE DIFFERENTIATION IN LEUKEMIA SUSCEPTIBLE MICE: STUDIES ON BONE MARROW AND THYMIC CHIMERAS.

Zielinski CC, Waksal SD, Datta SK
(c/o Datta), Cancer Res. Center, Tufts Univ. Sch. Medicine, Boston, MA, 02111
J Immunol; 129(2):882-889 1982

In the leukemia-prone AKR thymus, ecotropic and xenotropic-related viruses are expressed that generate leukemogenic recombinant viruses before the onset of leukemia. We have shown previously that (AKR x NZB)F1 hybrid mice do not develop leukemia because they severely restrict the expression of these retroviruses in their thymuses. The thymic microenvironment of the (AKR x NZB)F1 mice appeared to be of particular importance in determining this restriction, which was specified by an NZB-derived genetic influence. In the present study we analyze reciprocal thymus graft and irradiation bone marrow chimeras to establish that this influence is exerted by thymic reticuloepithelial cells. Prospective studies with thymic epithelial grafts from young mice show that the AKR thymic epithelium can simultaneously induce the amplified expression of retroviral genes, and changes in patterns of thymocyte differentiation that precede the development of leukemia, whereas the (AKR x NZB)F1 thymic epithelium is deficient in this regard. (Author abstract) (53 Refs)

37. ISOLATION OF MALIGNANT AND FUNCTIONAL LY 1+ T-CELL CLONES FROM B-CELL LYMPHOMAS.

Reinisch CL, Sing AP, Waldron JA, Kemp JD
Dept. Comparative Medicine, Tufts Univ. Sch. Veterinary Medicine, Boston, MA, 02111
Nature; 298(5870):176-178 1982

A unique model of a murine sarcoma virus (MSV)-induced B-cell lymphoma which is closely associated with a population of pre-malignant or malignant helper T cells was discovered in selected C57BL/6(B6) mice. Three-wk-old mice were injected im with 6 x 10(3) focus-forming units of murine sarcoma-murine leukemia virus (MSV). Those that developed a palpable tumor after 21 days were observed for more than 2 yr, during which time 15/17 developed mesenteric lymphadenopathy. Cell suspensions prepared from an enlarged mesenteric lymph node were injected into normal mice; all developed splenic and lymph node tumors 3 mo later. The transplantable tumor, called STC, produced progressive expansion of the splenic white pulp and of the paracortical and medullary cord areas of lymph nodes. The tumor infiltrates consisted mostly of small lymphocytic cells with varying degrees of plasmacytoid differentiation. Frequent PAS-positive cytoplasmic and intranuclear inclusions were present. An attempt to transfer STC with B cells resulted in Ly 1+ T cells instead; eleven clones produced the same way had the phenotype Thy 1.2+ (monoclonal antibody 30 H12), Ly 1+, Ly 2-. Doses of one clone injected into B6 mice resulted in rapid death due to immunoblastic T-cell sarcoma, morphologically distinct from the plasmacytoid lymphocytic lymphomas induced by MSV, STC, or B cells. Reverse hemolytic plaque assay demonstrated the ability of these clones to enhance Ig secretion by plasma cells in the absence of antigen. (14 Refs)

38. ANTIGENIC AND CHROMOSOMAL CHANGES IN THYMUS AND SPLEEN OF BALB/MO MICE DURING LEUKEMOGENESIS.

Asjo B, Fenyo EM, Spira J
Dept. Tumor Biology, Karolinska Institutet, S 104 01 Stockholm, Sweden
Leuk Res; 6(3):413-419 1982

Correlation between the amplification of the Moloney murine leukemia virus (M-MuLV) and appearance of M-MuLV induced cell surface antigen, MCSA, on thymus cells was studied in Balb/Mo mice. Production of infectious virus in the preleukemic mice was accompanied by the appearance of viral p30 antigen on the surface of thymus cells. All organs of Balb/Mo mice were negative for MCSA up to 40 days. Thereafter occasional thymuses contained a low fraction of MCSA-positive cells. Thus, Balb/Mo mice differed from mice neonatally inoculated with M-MuLV since the amplification of the

viral genome was not accompanied by the appearance of MCSA on thymus cells. Mice mainly developed lymphomas with two distinct clinical manifestations. One type was characterized primarily by enlargement of spleen and lymph nodes, and the other by enlargement of thymus with eventual infiltration of peripheral lymphatic organs. Leukemia latency varied between 3-10 mo and was not correlated with any particular type of lymphoma. Thymus cells were often MCSA positive while spleen cells of the same animal were MCSA negative. Based on the antigen patterns of thymomas and lymphomas, Balb/Mo lymphoma mice were more often negative for MCSA (68%) than mice receiving M-MuLV at birth (40%). The majority of thymus cells was MCSA positive while the spleen was MCSA negative. No correlation between the antigen expression and chromosome constitution could be observed. Amplification of the M-MuLV genome in young Balb/c mice was not accompanied by the appearance of MCSA on thymus cells. Results suggested that MCSA is related to a virus activated in a minority of Balb/Mo mice during the late phase of leukemogenesis. (14 Refs)

39. GENETIC CONTROL OF MURINE LEUKEMIAS INDUCED BY MOLONEY VIRUS.

Debre P, Gisselbrecht S, Boyer B, Levy JP
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Bull Cancer (Paris); 69(2):178-187 1982

The genetic control of leukemias was established in mice of different inbred strains inoculated with Moloney leukemia virus M-MuLV. To characterize the different steps of the host virus relationship, the degree of viremia, the appearance of leukemia, organ involvement, and the surface phenotype of leukemic cells were determined in individual mice. Immunological responses of those mice were studied by comparing the antibody production against virus or infected cells, and cytolytic T cell (CTL) responses. The results demonstrate that: (a) the viremia was controlled by H-2 and non H-2 genes. Three Rmv H-2 genes were located in the I and D or T region of the MHC. These genes behave like immune response genes controling the specific antiviral antibody production. D region Ir gene(s) also controlled the CTL but apparently differed from the Rmv genes. In addition to H-2 genes other gene(s) mapped outside the complex affected the virus production; (b) non H-2 genes which were not involved in viremia control, were determinant in the induction of malignancies since some sensitive strains never became leukemic despite high level of viremia; (c) the anatomical type of Moloney virus induced leukemias varied according to the non H-2 background since Thymus or spleen involvement differed in B10 and BALB congenic mice; (d) in a given inbred strain, the leukemia arising in different animals frequently expressed different phenotypes. It can be concluded that Moloney virus induced leukemia is a multistep process. H-2 Ir genes control the antiviral-antibody responses. However, the mode of action of other non H-2 genes is still unknown. (Author abstract) (25 Refs) (In FRE)

40. EXPRESSION OF ENDOGENOUS VIRAL GENES IN MOUSE LYMPHOCYTES.

Wecker E, Horak I
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Curr Top Microbiol Immunol; 98:27-36 1982

The association of expression of endogenous viral genes of xenotropic origin with immunological phenomena in mice and chickens is discussed. Xenotropic murine leukemia virus (X-MuLV) genes are present in all strains of mice. Viral gene products, such as X-MuLV gp70, may be expressed spontaneously or after stimulation by mitogens or antigens. In some strains of mice, stimulation of B-lymphocytes by mitogens leads to differentiation to immunoglobulin-producing cells, accompanied by production of C-type virus particles. T-cells can also be stimulated to express MuLV gp70 and env gene products. X-MuLV gp70 is expressed to widely varying degrees by lymphocytes from greater than 100 strains of mice studied. Stimulation by B- or T-cell mitogens enhances this expression. In most strains of mice expression of env genes is predominantly repressed. Activation of lymphocytes results in derepression of env genes. Some evidence suggests that gp70 or other X-MuLV gene products may play some role in normal physiological processes in mice and chickens. Several studies indicate that both mouse and chicken proviral sequences have long 5' and 3' terminal repeats (LTR). These LTR are capable of promoting transformation. If X-MuLV viruses have similar promoting activity, LTR may be more important than structural viral genes in promoting growth and/or differentiation of host cells, particularly lymphocytes. (24 Refs)

41. AN IMMUNOLOGICAL ANALYSIS OF ABELSON VIRUS-INDUCED LYMPHOMAS.

Grunwald DJ
The University of Wisconsin, Madison, WI
Diss Abstr Int [B]; 42(6):2225-B 1981

Lymphomas were induced in C57BL/6 and BALB/c mice by either of two strains of the Abelson murine leukemia virus (A-MuLV). The tumors, and clonal lines derived from them, were examined before and after in vivo growth in genetically distinguishable host mice for the expression of biochemical and biological markers associated with A-MuLV-transformed cells. All tumors and clonal lines initially expressed an A-MuLV-encoded protein. Lymphomas induced by NIH A-MuLV expressed a serologically related 'gag-fusion' protein of 160,000 daltons (p160). After several weeks of propagation in vivo as ascites tumors, all tumors and clonal lines ceased synthesis of the A-MuLV-encoded proteins. One clonal line that initially synthesized p160 has been studied in detail. By the seventh in vivo transplant generation in genetically distinguishable host mice, this tumors line showed no evidence of synthesis of the A-MuLV-encoded protein. Cells from this tumor line were then placed back into tissue culture and recloned. All p160-negative clones derived in this manner continued to express the alloantigenic marker H-2b and the isoenzyme gp-1b of the donor tumor cells, indicating that these cells were of donor and not host origin. Examination of cellular DNA obtained from p160-positive and derivative p160-negative lines indicated that the p160-negative clones had lost all A-MuLV-specific proviral sequences. Although the clonal lines lost the A-MuLV genome upon in vivo propagation, they retained their malignant phenotype and continued to express the Abelson lymphoma antigen, a cell surface marker associated with A-MuLV-induced lymphomagenesis. Several cellular phenotypic changes occurred concurrently with the loss of the A-MuLV provirus from the Abelson lymphoma cells. Whereas the progenitor p160-positive clonal line lacked detectable markers of mature T lymphocytes, the derivative p160-negative clonal lines expressed the Thy-1 and Lyt-1 antigens associated with cells of the T lymphocyte lineage. (no Refs)

42. HYPERPLASTIC AND NEOPLASTIC ERYTHROPROLIFERATIVE DISEASES INDUCED BY ONCOGENIC MURINE RETROVIRUSES.

Scolnick EM
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Biochim Biophys Acta; 651(4):273-283 1982

Structure of Harvey (HV) and Kirsten virus (KV), transforming protein of HV and KV, and Friend virus complex are discussed. Comparison of polycythemia- and anemia-inducing strains of spleen focus-forming virus (SFFV) is presented. Friend murine leukemia virus-induced (F-MuLV) disease and pathophysiology of F-MuLV-induced disease are described. Possible pathophysiological relationships between Friend virus-induced erythoproliferation and Harvey sarcoma virus (Ha-SV)-induced erythroleukemia are discussed. Biochemistry of transforming proteins of erythroleukemia viruses is reviewed. One possible advantage that studies of erythroleukemia have is that the abnormal proliferation of erythroid precursor cells induced by SFFV or Ha-SV is accompanied by a decreased requirement by these cells for erythropoietin. Studies on erythroid cells are limited by the availability of large quantities of purified erythropoietin. Both polycythemia-inducing SFFV and Ha-SV induce the abnormal proliferation of fully hemoglobinized erythroid colonies in cell culture colony assays for the viruses. Results might suggest that Ha-SV infection of stem cells could be a method for generating stem cell lines. (81 Refs)

43. MODULATION OF ERYTHROPOIESIS BY THE HELPER-INDEPENDENT FRIEND LEUKEMIA VIRUS F-MULV.

Nibo Y, Shibuya T, Mak TW
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J Exp Med; 156(1):146-158 1982

Modulation of erythropoiesis in newborn and adult BALB/c mice and adult DBA/2 mice by a replication-independent leukemia virus (F-MuLV) in Friend erythroleukemia virus (FLV) was investigated. Colony-forming unit-erythroid (CFU-E) and burst-forming unit-erythroid (BFU-E) progenitor colony assays were performed following virus infection. A dramatic increase in BFU-E-like colonies was observed in 1-day-old BALB/c mice infected with 3 x 10(5) XC plaque units of F-MuLV, while CFU-E did not increase. BFU-E-like colonies reached a level of approx 1,500 bursts/10(5) cells or approx 5 x 10(7) BFU-E/spleen. Erythropoietic changes were induced in adult DBA/2 or BALB/c mice when phenylhydrazine (PHZ) was administered in conjunction with F-MuLV. Injection of F-MuLV into PHZ-treated adult mice induced splenomegaly, a decrease in hematocrits, and enhancement of levels of CFU-E. Thus, F-MuLV, without spleen focus-forming virus, can modulate erythropoiesis in newborn and adult mice. Induction of a dramatic increase in BFU-E without an increase in CFU-E implies that the leukemic block in F-MuLV-infected newborn mice is at a stage between BFU-E and CFU-E. These results suggest that F-MuLV may infect different erythroid target cells than the FLV complexes. (39 Refs)

REVIEWS AND OTHER RELATED STUDIES

44. SURFACE MARKERS ON LEUKEMIA AND LYMPHOMA CELLS: RECENT ADVANCES.

Foon KA, Schroff RW, Gale RP
Biological Response Modifiers Program, NCI-Frederick Cancer Res. Facility, Building 560, Frederick, MD, 21701
Blood; 60(1):1-19 1982

Recent advances in immunology have led to important insights into leukocyte differentiation and the cellular origin of leukemia. It is now possible to precisely define stages of human lymphocyte and granulocyte differentiation utilizing highly specific monoclonal antibodies that define cell surface antigens in conjunction with more traditional markers such as surface and cytoplasmic immunoglobulin on B lymphocytes, sheep erythrocyte (E) receptors on T lymphocytes, and cytochemical staining of myeloid cells. Five major subtypes of acute lymphoblastic leukemia (ALL) are now recognized, including unclassified or null ALL, common ALL (cALL), pre-B-ALL, B-ALL, and T-ALL. Within the T-ALL subgroup, there is considerable heterogeneity based on the presence or absence of the E-receptor and various T-cell surface membrane antigens defined by monoclonal antibodies. Cells from patients with chronic lymphocytic leukemia, non-Hodgkin's lymphoma, and Sezary syndrome also can be classified by their reactivity with monoclonal antibodies. Acute myelogenous leukemia (AML) cells are generally classified by morphological and cytochemical features. Recently, monoclonal antibodies reactive with granulocytic and monocytic subtypes of AML have been developed. In addition to their utility in leukemia classification, monoclonal antibodies that identify leukemia associated antigens have also been used therapeutically. Monoclonal antibodies have been infused intravenously into patients with leukemia and lymphoma. They have also been used in vitro with complement to lyse residual leukemia cells from remission bone marrows removed from leukemia patients. These treated bone marrows were later reinfused into the same patients to 'rescue' them following high-dose chemotherapy and radiation therapy. (Author abstract) (203 Refs)

45. BURKITT'S LYMPHOMA.

Ziegler JL
Veterans Admin. Medical Center, San Francisco, CA
CA; 32(3):144-161 1982

Etiology, clinical features, staging, treatment, and immunology of Burkitt's lymphoma are reviewed. Most, but not all cases are associated with Epstein-Barr virus (EBV); the causative role of EBV, if it exists, may be related to differences in viral strains. In addition to EBV, genetic factors, immunoregulatory determinants related to environment, and possibly an RNA virus have also been suggested as causes. Systemic chemotherapy is the treatment of choice. After complete remissions lasting about 1 yr, recurrence is rare. Prognosis is directly related to the tumor burden upon initial presentation. Burkitt's lymphoma is one of a dozen neoplasms that can be cured by drugs alone. It is the most likely candidate for a virus-induced human tumor. Studies of the association of Burkitt's lymphoma and EBV led to the discovery of EBV as the cause of infectious mononucleosis. Experimental and clinical studies of Burkitt's lymphoma have led to important advances in immunobiology and tumor immunology. Promising approaches in immunotherapy include rapid removal of antigen excess and immune complexes from the circulation and enhancement of normal immunoregulatory controls of the body. (121 Refs)

46. POSSIBLE IMMUNOLOGICAL MECHANISMS IN C-TYPE VIRAL LEUKEMOGENESIS IN MICE.

Ihle JN, Lee JC
Biological Carcinogenesis Program, Frederick Cancer Res. Center, Frederick, MD
Curr Top Microbiol Immunol; 98:85-101 1982

The role of C-type viruses in leukemogenesis in mice is reviewed. The mechanisms by which C-type viruses induce leukemia are distinct from those by which the same type of viruses induce sarcomas. In leukemogenesis the viruses are replication-competent, nontransforming, and do not contain additional cellular pathogenic sequences. Latency periods are longer for leukemia than for sarcomas. Induction of leukemia is associated with acute viremia. Studies in mice indicate cellular immune response is an integral part of the process of leukemogenesis. Among the specific components of the leukemogenic process is the absolute requirement for antigen-specific lymphocytes. Preleukemic states involve chronic immune stimulation that is not limited to antigen-specific components but includes systemic effects. A proposed model suggests that immune stimulation is required to provide targets for viral infection and transformation. A second model describes a unique interaction of virus with antigen-specific cells to produce transformation. In a third proposed model, chronic immune stimulation produces somatic errors, which result in transformation leading to leukemia. Experimental approaches are available for future research to clarify the mechanisms of viral leukemogenesis. (63 Refs)

47. RETROVIRUS LYMPHOMAGENESIS: RELATIONSHIP OF NORMAL IMMUNE RECEPTORS TO MALIGNANT CELL PROLIFERATION.

Weissman IL, McGrath MS
Lab. Experimental Oncology, Dept. Pathology, Stanford Univ. Sch. Medicine, Stanford, CA, 94305
Curr Top Microbiol Immunol; 98:103-112 1982

The hypothesis that the principal reason for proliferation of cells transformed by slowly transforming retroviruses is due to stimulation by their antigen-specific receptor-mitogen complex is proposed. The oncogene should be the viral env gene, not a host cellular gene. Experimental evidence is reviewed which illustrates the following: each T cell lymphoma expresses surface receptor highly specific for the retrovirus which is produced by it; receptor recognition specificity maps to the env region; the virus receptor is a marker for leukemia cells and distinguishes them from preleukemic cells in the same thymus; virus receptor binding may regulate lymphoma proliferation; and virus receptors on lymphoma cells can be antigen-specific receptors. Taken together, the results provide strong evidence for a receptor-mediated leukemogenesis hypothesis (RMLH). A comparison of this hypothesis with the chronic immunostimulation hypothesis (CIH) demonstrated the following differences: CIH requires a second genetic event within the stimulated host cell before lymphoma generation can occur, while RMLH does not; in CIH, the preleukemic cells switch from antigen-responsive behavior to growth factor-responsive behavior; with CIH the proliferating cells in the preleukemic period appear to be responsive to gp70, while the RMLH model indicates a specificity controlled by sequences within p15E and/or the R region; and CIH concerns mitogen responsiveness of the spleen population, while RMLH follows receptor binding specificities of thymus cells and intrathymic lymphomas. (21 Refs)

48. PERSPECTIVES ON ENDOGENOUS RETROVIRUSES IN NORMAL AND PATHOLOGICAL GROWTH.

Weiss RA
Inst. Cancer Res., Fulham Road, London SW3 6JB, England
Curr Top Microbiol Immunol; 98:127-132 1982

The origin and persistence of endogenous retroviruses, normal functions of endogenous viruses, and viral leukemogenesis are reviewed. The endogenous viral elements studied in extant hosts are guilty of infection before their adoption by the germ line. The number, structure, and location of endogenous viral elements in individual hosts are variable due to substantial population polymorphism. Xenotropism is discussed. Endogenous proviruses are not significantly harmful to the host population. Env gene products may control intercellular signals involving interleukins and other lymphokines in certain species, but may not be universal. Intercellular communication may change from species to species. In some species endogenous retrovirus genes may have a useful lymphoid function. Except for certain high cancer strains of mice, endogenous retroviruses are not known to be pathogenic. An endogenous virus may evolve leukemogenic properties on exogenous passage, and the presence of endogenous sequences may protect the host from the oncogenic effect of a related exogenous virus. Low or nonleukemogenic endogenous viruses may be distinguished from the more potently oncogenic recombinant or exogenous relatives by the 3'-end of the genome, either in the env gene or the adjacent retrovirus flanking sequences. The latter region, rather than the env determines oncogenicity. The preneoplastic transformation of bursal follicles occurs faster and more often than the final, clonal development of metastatic lymphoma in chickens. Two hypotheses on leukemogenesis are described. (38 Refs)

49. THE PATHOGENESIS OF ABELSON VIRUS LYMPHOMAS OF THE MOUSE.

Risser R
McArdle Lab. for Cancer Res., Univ. Wisconsin, Madison, WI, 53706
Biochim Biophys Acta; 651(4):213-244 1982

The origin of the Abelson virus (AV) and the pathogenesis of the disease it induces are discussed. Before discussing Abelson murine leukemia virus (A-MuLV) in detail, some insights gained from the study of other RNA tumor viruses, both with respect to mechanisms of their action and host genetic responses to them, are presented. The main presentation comprises four sections. Virological and molecular characterization of AV involves its isolation, assays, genome structure of the helper and defective viruses, proteins encoded by the defective A-MuLV genome, and mutants of AV. Biology of AV diseases is discussed in relation to transformation of bone marrow cells by A-MuLV and pathogenesis. Differentiative phenotype of Abelson lymphomas and cell lines is discussed in relation to phenotypes of in vitro-derived lines, expression of lineage markers by tumors, and neoplastic differentiation of clonal Abelson lymphoma lines. With relation to cellular antigens identified on Abelson lymphoma and transformed cells, Abelson target-associated antigen, p50 and Abelson lymphoma antigens are discussed. A final section presents a summary of present knowledge, interpretations and further speculations on the involvement of AV in hematopoietic differentiation and neoplasia. (187 Refs)

50. AVIAN LEUKEMIA VIRUSES ONCOGENESES AND GENOME STRUCTURE.

Graf T, Stehelin D
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Biochim Biophys Acta; 651(4):245-271 1982

Avian leukemia viruses, with emphasis mainly on defective leukemia viruses (DLVs), are reviewed. Oncogenic spectra of chicken-derived DLVs and the turkey-derived reticuloendotheliosis virus (REVT) are presented. Transformation specificity of DLVs in vitro, genetic content and genome structure of avian erythroblastosis virus (AEV), avian myeloblastosis virus (AMV)-type, myelocytomatosis virus strain 29 (MC29)-type, REVT, expression of RNA and proteins in cells infected with AEV, AMV, MC29, and OK10, genetics of DLVs including mutants in transforming functions and recovered viruses, conservation of cellular oncogene (c-onc) genes through evolution, chromosomal localization and structure of c-onc genes, and expression of c-onc genes in normal cells, mechanisms of transformation by avian leukosis viruses (ALV) and DLVs, the promoter insertion hypothesis of ALV-leukemogenesis, hematopoietic target cell specificity and possible role of c-onc genes in the DLV-leukemogenesis, and transformation of nonhematopoietic cells by DLVs are discussed. Origin of DLVs is reviewed, including reverse transcription of encapsidated viral and cellular RNAs, viral promoter insertion, recombination of integrated provirus with a c-onc gene, and integration of proviruses around a c-onc gene. (167 Refs)

51. BIOLOGICAL CARCINOGENESIS.

Rich MA, Furmanski F
AMC Cancer Res. Center and Hosp., Lakewood, CO
Biological Carcinogenesis. New York, Marcel Dekker, Inc., 310 pp., 1982.

The general principles which govern carcinogenesis are identified for each of the major classes of carcinogens and the extent these principles are applicable to the carcinogenic process induced by other classes of agents is determined. Current knowledge on the interaction of carcinogens and the identification of biological systems where viral, chemical, and physical carcinogens are demonstrably interactive are described. Mechanisms in viral carcinogenesis are discussed with respect to: T-cell growth, T-cell growth factor, T-cell leukemias and lymphomas and isolation of a new type-C retrovirus, properties of sarcoma growth factors produced by sarcoma virus transformed cells, and interactions of murine leukemia viruses with hematopoietic stem cells. Mechanisms in chemical carcinogenesis are discussed with respect to activation of carcinogenic polycyclic hydrocarbons by metabolism, involvement of a protein kinase in multistage skin tumor promotion, and the effect of tumor-causing chemicals on the control of mutagenesis and differentiation in mammalian cells. Transformation of cloned mammary epithelial cells following combined treatment with mouse mammary tumor virus and dimethylbenz(a)anthracene, virus-cell interactions during hormonal carcinogenesis, and separate pathways for viral and chemical carcinogenesis in the mouse mammary gland are described. A molecular approach to studies of chemical carcinogen-virus interaction is presented. Other presentations deal with multistage recombinational origin of leukemogenic viruses, radiation-induced leukemogenesis, neoplastic transformation of cultured cells by herpes simplex virus type 2 and carcinogens, modulation of adenovirus transformation and replication, and transformation of murine fibroblasts. (682 Refs)

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1. ASBESTOS CARCINOGENESIS: ASBESTOS INTERACTIONS AND EPITHELIAL LESIONS IN CULTURED HUMAN TRACHEOBRONCHIAL TISSUES AND CELLS.
Haugen A, Harris C
Div. Cancer Cause and Prevention, NCI, Bethesda, MD
Recent Results Cancer Res; 82:32-42 1982

2. REVIEW: ORAL CONTRACEPTIVES AND MENOPAUSAL ESTROGENS IN RELATION TO BREAST NEOPLASIA.
Brzezinski A, Schenker JG
Dept. Obstetrics and Gynecology, Hadassah Univ. Hosp., POB 12000, 91120 Jerusalem, Israel
Isr J Med Sci; 18(4):433-438 1982

3. LIVER DISEASES DUE TO HORMONAL CONTRACEPTIVES.
Lie TS
Chirurgische Klinik und Poliklinik, Universitat, Sigmund-Freud-Str. 25, D-5300 Bonn 1, W. Germany
MMW; 124(20):489-494 1982
In GER

RADIATION CARCINOGENESIS

4. THE WORK OF THE NRPB 1977/80 AND A REVIEW OF THE FIRST 10 YEARS.
National Radiological Protection Board
Natl. Radiological Protection Board, Chilton, Didcot, Oxfordshire OX11 0RQ, England
The Work of the NRPB 1977/80 and a Review of the First 10 Years. Chilton, Didcot, Oxfordshire, National Radiological Protection Board, 70 pp., 1981.

DIETARY FACTORS IN CARCINOGENESIS

5. ALCOHOL AND CARCINOGENESIS.
Seitz HK, Czygan P, Kommerell B
Schwerpunkt Gastroenterologie, Medizinische Universitatsklinik, Bergheimer Str. 58, D-6900 Heidelberg 1, W. Germany
Leber Magen Darm; 12(3):95-107 1982
In GER

6. ZINC, COPPER, AND MANGANESE IN IMMUNE FUNCTION AND EXPERIMENTAL ONCOGENESIS.
Beach RS, Gershwin ME, Hurley LS
Dept. Internal Medicine, Div. Rheumatology-Clinical Immunology, Univ. Calif., Davis, CA, 95616
Nutr Cancer; 3(3):172-191 1982

EPIDEMIOLOGY, ETIOLOGY AND GENETIC ASPECTS OF HUMAN CANCER

7. TRENDS IN CANCER INCIDENCE: CAUSES AND PRACTICAL IMPLICATIONS. PROCEEDINGS OF A SYMPOSIUM HELD OSLO, NORWAY, 6-7 AUGUST 1980.
Magnus K
The Cancer Registry Norway, Montebello, Oslo 3, Norway
Trends in Cancer Incidence: Causes and Practical Implications, Proceedings of a Symposium held Oslo, Norway, 6-7 August 1980. Washington, D. C., Hemisphere Publishing Corporation, 446 pp., 1982.

ENVIRONMENTAL AND OCCUPATIONAL FACTORS IN CARCINOGENESIS

8. QUANTIFICATION OF OCCUPATIONAL CANCER.
Peto R, Schneiderman M
Nuffield Dept. Clinical Medicine, Radcliffe Infirmary, Univ. Oxford, Oxford, England
Banbury Rep (9): 756 pp., 1981.

9. NASAL CARCINOMA IN WOODWORKERS: A REVIEW.
Wills JH
Sch. Medicine, Uniformed Services Univ. Health Sciences, 4301 Jones Bridge Road, Bethesda, MD, 20814
JOM; 24(7):526-530 1982

10. AIR POLLUTION AND CANCER. A REVIEW OF EXPERIMENTAL INVESTIGATIONS.
Madsen ES, Nielsen PA, Pedersen JC
(c/o Nielsen), Stigardsvej 2, DK-2900 Hellerup, Denmark
Ugeskr Laeger; 144(23):1719-1721 1982
In DAN

11. AIR POLLUTION AS A RISK FACTOR IN LUNG CANCER.
Vena JE
Dept. Social and Preventive Medicine, State Univ. New York at Buffalo, 2211 Main St., Buffalo, NY, 14214
Am J Epidemiol; 116(1):42-56 1982

12. INHALATION CARCINOGENESIS: AN OVERVIEW.
Chretien J
Hopital Laennec, 42 rue du Sevres, F-75007 Paris, France
Recent Results Cancer Res; 82:1-10 1982

13. THE NITROSAMINE HAZARD.
Yonkers AJ
Dept. Otolaryngology, Univ. Nebraska, Omaha, NE
Ear Nose Throat J; 61(7):407-414 1982

CELLULAR AND MOLECULAR MECHANISMS IN CARCINOGENESIS

14. ONCOGENES OF SPONTANEOUS AND CHEMICALLY INDUCED TUMORS.
Weinberg RA
Center for Cancer Res., Massachusetts Inst. Technology, Cambridge, MA, 02139
Adv Cancer Res; 36:149-163 1982

15. RELATIONSHIP OF DNA TERTIARY AND QUATERNARY STRUCTURE TO CARCINOGENIC PROCESSES.
Lipetz PD, Galsky AG, Stephens RE
Dept. Radiology, Ohio State Univ., Columbus, OH, 43210
Adv Cancer Res; 36:165-210 1982

16. ROLE OF ENZYMATIC METHYLATION OF DNA IN CELL DIFFERENTIATION AND TRANSFORMATION.
Fedorov NA
Central Res. Inst. Hematology and Blood Transfusion, Moscow, USSR
Eksp Onkol; 4(3):3-11 1982
In RUS

17. HYDROGEN ION DYNAMICS AND CANCER: AN APPRAISAL.
Harguindey S
Dept. Thoracic Surgery and Oncology, Roswell Park Memorial Inst., 666 Elm St., Buffalo, NY, 14263
Med Pediatr Oncol; 10(3):217-236 1982

MODIFICATION OF CARCINOGENESIS

18. CARCINOGENESIS AND BIOLOGICAL EFFECTS OF TUMOR PROMOTERS.
Hecker E
Inst. Biochemistry, German Cancer Res. Center, Heidelberg, W. Germany
Carcinogenesis 7: 664 pp., 1982.

VIRAL AND IMMUNOLOGICAL ASPECTS OF CARCINOGENESIS

19. AVIAN LEUKEMIA VIRUSES: ONCOGENESES AND GENOME STRUCTURE.
Graf T, Stehelin D
Inst. Virology, German Cancer Res. Center, In Neuenheimer Feld 280, 6900 Heidelberg, W. Germany
Biochim Biophys Acta; 651(4):245-271 1982

20. HYPERPLASTIC AND NEOPLASTIC ERYTHROPROLIFERATIVE DISEASES INDUCED BY ONCOGENIC MURINE RETROVIRUSES.
Scolnick EM
Lab. Tumor Virus Genetics, NCI, Bethesda, MD, 20205
Biochim Biophys Acta; 651(4):273-283 1982

METHODOLOGY IN CARCINOGENESIS RESEARCH

21. MOLECULAR EPIDEMIOLOGY AND CARCINOGEN-DNA ADDUCT DETECTION: NEW APPROACHES TO STUDIES OF HUMAN CANCER CAUSATION.
Perera FP, Weinstein IB
Div. Environmental Sciences, Columbia Univ., New York, NY, 10032
J Chronic Dis; 35(7):581-600 1982

22. AN EVALUATION OF ASSAY PROCEDURES FOR DETECTION OF TUMOR PROMOTORS.
Sivak A
(c/o P. H. Lohman) Medical Biological Lab. TNO, P.O. Box 45, 2280 AA Rijswijk, The Netherlands
Mutat Res; 98(3):377-387 1982

23. DNA REPAIR ASSAYS AS TESTS FOR ENVIRONMENTAL MUTAGENS. A REPORT OF THE U.S. EPA GENE-TOX PROGRAM.
Larsen KH, Brash D, Cleaver JE, Hart RW, Maher VM, Painter RB, Sega GA
Environmental Mutagen Information Center, Oak Ridge Natl. Lab., Oak Ridge, TN, 37830
Mutat Res; 98(3):287-318 1982

24. AN EVALUATION OF THE HOST-MEDIATED ASSAY AND BODY FLUID ANALYSIS. A REPORT OF THE U.S. ENVIRONMENTAL PROTECTION AGENCY GENE-TOX PROGRAM.
Legator MS, Bueding E, Batzinger R, Connor TH, Eisenstadt E, Farrow MG, Ficsor G, Hsie A, Seed J, Stafford RS
Dept. Preventive Medicine and Community Health, Div. Environmental Toxicology, Univ. Texas Medical Branch, Galveston, TX, 77550
Mutat Res; 98(3):319-374 1982

25. THE PHYSIOLOGICAL IMPORTANCE OF THE COLONIC MICROFLORA.
Gustafsson BE
Dept. Germfree Res., Karolinska Inst., Box 60 400, S-104 01 Stockholm, Sweden
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26. AN ASSESSMENT OF THE ROLE OF MICRODOSIMETRY IN RADIOBIOLOGY.
Goodhead DT
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27. PSYCHOSOCIAL ASPECTS OF CANCER.
Cohen J, Cullen JW, Martin LR
Sch. Social Welfare, Univ. California, Los Angeles, Los Angeles, CA
Psychosocial Aspects of Cancer. New York, Raven Press, 320 pp., 1982.

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